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(1) Hanson, I. R. and Hingson, R. A., *Current Researches in Anesthesia and Analgesia,* 29:136 (May-June) 1950.

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EBBS AND FLOWS IN MEDICAL INTEREST

HENRY A. CHRISTIAN, M.D.*

AS one grows old in medicine, he recalls ebbs and flows in the tides of medical interest in various diseases, as evidenced by periods when many articles are published on some specific subject and other periods when interest in that subject seems to wane for months or even years. In the course of time one can even observe an irregular periodicity of these cycles and mentally plot curves of ebb and flow. The full cycle is occasionally as short as five years; occasionally it lasts ten or fifteen years, or even longer.

It is stimulating to try to evaluate the significance of such curves of incidence, since this must involve not alone knowledge of and interest in a disease and its management but also a contact with much collateral activity in that field of medicine. Sometimes I have been able to say to the young men gathered with me about the bedside of a patient that very likely numerous papers on this disease would shortly appear, as the ebb tide of interest had run its expected course and the flood tide would soon return. I have found myself wondering why these ebbs and flows in medical interest exist, when the prevalence of the specific disease remains unchanged, and what goes on with regard to these subjects during the periods when the tide is ebbing. This meditative pastime becomes all the more interesting when the cycles have occurred several times in one's own lifetime. Obviously the causes initiating a recrudescence of interest are usually multiple.

My own contacts with and interest in acute idiopathic pericarditis are illustrative of what I have in mind. Recently there have appeared several papers on this topic with a variation in terminology — the word idiopathic, for example, variously expressed as benign, cryptic, primary, epidemic, nonrheumatic, nonspecific, relapsing, fugitive or of undetermined cause. Apparently two factors have influenced this recent flow of papers: the prevailing interest in the electrocardiogram distinctive of pericarditis and the assumed difficulty in determining that the pericarditis recognized by physical examination was not a sequence to infarction of the myocardium, another topic in which great interest has currently been shown. Besides emphasizing these factors, recent papers have been largely descriptive of the clinical manifestations of this type of pericarditis and have presented results of those laboratory examinations usually made in the study of acute infectious disease. Except for the descriptions of the electrocardiograms, these papers have added little or nothing to what had appeared in the papers of a previous period of journalistic interest.

When these recent papers began to appear, it seemed to me that they were descriptive of a familiar condition, one so generally understood and recognized as scarcely to need discussion at the present time. I recalled patients that I had seen with this type of pericarditis correctly diagnosed twenty-five years ago. I had even published a book in 1930, *Diagnosis and Treatment of Diseases of the Heart*, in which I had included the classification of acute pericarditis of the idiopathic type and briefly described its characteristics, indicating interest in those cases with upper-abdominal pain, not infrequently misdiagnosed as some inflammatory condition of the abdomen needing surgical exploration.

In 1908 I began as Hersey Professor a series of comprehensive lectures on medicine to Harvard students, which for some time my secretary took down in shorthand and subsequently typed. In an early lecture on pericarditis, actually delivered in 1909, I spoke of idiopathic pericarditis, as an acute type of the disease; I described it and told my students that discussions of it would be found in their textbooks of medicine. This was correct, for numerous textbooks of that day included it — obvious evidence that this form of pericarditis had become incorporated in general medical knowledge; no special papers on it appeared in the journals of this period. Going back to my student days, I found idiopathic pericarditis described in the second edition of *Osler's Principles and Practice of Medicine*, which I had used as a student. Thus my familiarity with it really began in my student days in medicine, from 1898 to 1900, at Johns Hopkins.

Thus there had been a long period of ebb in the cycle of interest in acute idiopathic pericarditis, as it was then called. In that period no new technics of examination and no new knowledge had apparently been developed to inaugurate a flow of interest.

*The late Henry A. Christian was Hersey Professor of the Theory and Practice of Physic, emeritus, Harvard Medical School, and physician-in-chief, emeritus, at Peter Bent Brigham Hospital.

Going back into the literature, I have found that preceding this long ebb cycle there had been a flow cycle in the last third of the nineteenth century, with some dozen papers scattered along the way from 1854 to 1887, with the majority appearing between 1876 and 1882.

What had been responsible for the period of activity or interest productive of these papers on acute idiopathic pericarditis? Seemingly it was the previous general recognition that rheumatic fever was a frequent cause of heart disease, including acute pericarditis. This led to the use of the terminology — acute pericarditis caused by rheumatic fever, or rheumatic pericarditis. Soon, however, the clinicians of that day began to see patients with acute pericarditis in whom there was nothing to suggest an accompanying or preceding rheumatic fever, and consequently they separated another type and designated it as idiopathic. Incidentally, it seems that this designation, on the basis of priority in use, should still be used, rather than another of the various terms recently advocated. One can now prophesy, after a short period of ebb, a new flow of interest based on a probable demonstration of a viral etiology of this type of pericarditis, seemingly idiopathic, and on the use of antibiotics in its treatment.

Another example of ebb and flow in medical interest can be found in the history of typhoid fever. In this regard the cycles cover a longer period of time than was the case with acute idiopathic pericarditis; they have largely been cycles of interest in treatment, with quiescent periods of continuation of the treatment they adopted. The first period of interest is a remote one, in which bloodletting, purgation and emesis were the chief ways of treating all sorts of sickness, including typhoid fever. The literature of this long period consisted of books, some written in Latin, for medical journals scarcely existed at that time. Some of the later studies of this period were well controlled, as was that of James Jackson, Hersey Professor of the Theory and Practice of Physic at Harvard from 1812 to 1836. He was the first physician appointed to the new Massachusetts General Hospital, established in 1811. There he tested the treatment of typhoid fever with emetics, giving these drugs to patients in varying stages of their infection, comparing their effects on mortality and duration of fever in treated cases with those in similar controls, who received the same treatment except for the emetic. After tabulating these results he concluded that emetics, preferably given in the first week of typhoid fever, were beneficial, lowering mortality and shortening the course of the disease. His results are interestingly described in his *Letters to a Young Physician*, the young physician being his son, James Jackson, Jr., who himself died of typhoid fever in 1834, shortly after receiving his degree in medicine from Harvard.

A second cycle of interest in typhoid fever began with Louis's studies of the disease in Paris, described in his book *Recherches anatomiques, pathologiques et thérapeutiqes sur la maladie connue sous le nom de gastro-entérite, fièvre putride, adynamique ataxique typhoide, etc.*, published in 1829. This interest was continued by his students, who, scattering to other countries, had the opportunity of applying Louis's methods to the differentiation of typhoid from typhus fever. Louis could not do this in France, for of the two diseases only typhoid fever then existed in that country. In the United States Gerhard made this distinction in two papers published in the *American Journal of Medical Sciences* in 1836 and 1837.

Again after this period came an ebb in interest, to be replaced by a renewed flow following Eberth's discovery in 1880 of the causative bacterium of typhoid fever. Now the cycles of ebb and flow became of shorter duration.

The simultaneous reports in 1896 by Widal and by Grünbaum of diagnostic agglutination of the bacilli in typhoid fever, the studies of the histology of the disease made by Mallory in 1898 and the clinical studies of Osler and his associates at the Johns Hopkins Hospital in the period 1894 to 1900 precipitated a new wave of great interest. This wave gradually subsided, to rise again after Shaffer and Coleman reported their studies in 1909, a result of which was the high-calorie diet advocated by Coleman in 1917. In the interval between these studies Russell, in 1912, demonstrated the effectiveness of antityphoid vaccination in the United States Army. Here were vital interests, those of treatment and prevention.

Gradually, with the development of safe water supplies and the pasteurization of milk and its sanitary distribution, the incidence of typhoid fever rapidly decreased until it finally became a mere curiosity in most civilized countries, and interest in it as a disease almost ceased.

However, even under these circumstances, this ebb in the cycle of interest did not continue. Although the disease occurred infrequently and had a lowered mortality by reason of the high-calorie diet, a really effective treatment of typhoid fever was still lacking. Such treatment, however, soon followed the advent of the antibiotics and the reports made in 1949 of the marked effectiveness of chloramphenicol in the disease. This discovery ended a short ebb in the cycle of interest and started a cycle of renewed interest during which, in all probability, the different antibiotics will be properly evaluated, so that such cases of typhoid fever as do occur can be quickly cured.

One problem of typhoid fever so far has not been solved. That is the role of typhoid carriers in initiating outbreaks of the disease. It is to be hoped that papers dealing with the solution of this problem will comprise a final cycle of increased interest in typhoid fever.

It has been shown for typhoid fever that each flow phase in curves of ebb and flow of interest has had a definite cause, such as improvement in therapy, demonstration of etiology, better knowledge of pathology, methods for prevention and the finding of a cure, and that each of these interests has gradually waned, to be followed by an ebb cycle. Usually, with typhoid fever, each cycle has been of brief duration, except for those of early medical history, until the discovery in 1880 of its bacillary cause.

The history of Q fever may serve as still another example of cyclic ebb and flow in medical interest. With this disease the cycle shows a quickened tempo, as compared with those of idiopathic pericarditis and of typhoid fever. Q fever was first observed in Australia in 1933 by E. H. Derrick and reported by him in the *Medical Journal of Australia* as a "new fever entity" in 1937. In the next year the etiologic organism, considered at that time to be a rickettsia, was isolated. The clinical syndrome of Q fever was soon recognized over a wide area and was intensively studied. Ebbs in interest were brief, with new flows quickly stimulated by new observations. Its recognition and exact identification as an infection easily acquired by laboratory workers intensified interest in it and facilitated the investigation of its immunologic reactions. These were soon to be used both in diagnosis and in the study of its epidemiologic distribution in active and inactive and possibly its carrier phases. In a brief period the causative organism was studied thoroughly, was recognized as a coxiella rather than a rickettsia and was named *Coxiella burnettii*.

In its wide distribution Q fever, or *Coxiella burnettii* fever, with its cause determined and its immunologic reactions recognized, offered exceptional opportunity for epidemiologic investigations, which started a fresh flow of medical interest. Why its distribution was both geographically and locally wide soon became evident, for it was shown that contact infection from patient to patient, insect transmission, airborne distribution, frequency in cattle and goats and probably other animals, penetration of the infecting coxiella through intact skin and infection through raw milk from infected cows and possibly through undercooked meat could and did occur.

The clinical interest in Q fever stimulated by these interesting epidemiologic studies scarcely began to ebb before a new flow of clinical interest started, stimulated by reports of the successful therapeutic use of antibiotics, especially aureomycin and chloramphenicol.

A still newer flow of interest in Q fever should soon be initiated by the perfection of prophylactic immunization and the development of adequate and reasonably simple measures for prevention. In Q fever the cyclic ebb and flow of medical interest has occupied only fourteen years from its first clinical reporting in 1937 to the present.

There are other items of ebb and flow in medicine that are of interest to the clinician and deserving of his consideration, since a knowledge of them may influence his thought and possibly save him from errors of interpretation. Such an ebb and flow can be noticed in an apparent, possibly actual, variation in incidence of diseases that may be noted in a physician's practice or in hospital admissions. In my annual report for 1929 as physician-in-chief of the Peter Bent Brigham Hospital in Boston, I analyzed the number of admissions to the hospital in the years 1916, 1917, 1928 and 1929 of patients suffering from various diseases. I found that in this period patients with typhoid fever, lobar pneumonia and Bright's disease decreased in number, while those with pulmonary tuberculosis and chronic arthritis increased moderately (that is, from 45 to 93 and from 42 to 104 respectively), those with peptic ulcer increased greatly (from 25 to 111) and the number of those with heart disease rose markedly (from 307 to 610). In contrast to this, the admission of patients with acute articular rheumatism, anemia, cancer of the stomach, cirrhosis of the liver and gall-bladder disease varied little.

These figures of incidence of admissions occurred in a hospital in which there was no change in the number of medical beds, no change in staff organization, very little change in personnel and no conscious change in the policy of the physician-in-chief and his associates. Some of these changes coincide with known changes in incidence of certain diseases, such as the near-disappearance of typhoid fever from the community. This, however, is not always true; tuberculosis has tended to decrease in Boston and the surrounding towns but not in the Peter Bent Brigham Hospital. Cancer of the stomach and diabetes mellitus, thought to be increasing in the community, did not change in hospital incidence, while heart disease, although rising in community incidence, increased disproportionately in the hospital.

Various possible explanations of changes not related to communal incidence of a disease can be thought of as determinative of such changes as have just been noted. Special interest in a given disease on the part of the hospital staff or some new method of therapy might account for such differences. At the Peter Bent Brigham Hospital increasing interest has been manifested in chronic arthritis, anemia (with the advent of liver therapy) and ulcer of the stomach and duodenum, but the increase in patients with chronic arthritis was not great, that in patients with ulcer of stomach and duodenum was very great and in patients with anemia there was no change; hence, such explanations do not give the whole answer. Incidentally, it is not always apparent why given diseases increase, decrease or remain

unchanged in cities, states and countries, although a satisfactory explanation can usually be assigned.

Another interesting ebb and flow in medicine concerns itself with changes in the severity of illness caused by certain diseases — not related to improvements in methods of prevention or treatment or both. As an example in my lifetime I have observed a striking and rather steady decrease in the severity of rheumatic fever, although there seems to have been no corresponding decrease in the seriousness or frequency of valvular heart disease of rheumatic origin. Likewise, I have twice seen influenza change from a rather mild illness to a serious one of pandemic proportions of high fatality. Bright's disease also has seemed to lessen in the severity of its manifestations, in a way not to be explained by any great improvement in its therapy and at a time when antecedent, probably causative bacterial infections were no better controlled or treated. This occurred in the period prior to the use of sulfonamides and antibiotics in these infections.

Still another ebb and flow should be noted; this concerns the use of therapeutic agents. As an example, forms of treatment have been recommended for pernicious anemia and reported with enthusiasm, until the efficient use of liver preparations and adjunctive treatment stopped this therapeutic flow. We have also seen ebbs and flows in the use of iron for anemias, from a period when great effectiveness was noted, as when chlorosis was a common disease, to a period during which it was regarded as hardly more than a tonic, with a return to the more recent recognition of its effectiveness in the hypochromic or iron-deficiency anemias. We have seen digitalis, recognized by William Withering as effective in treating dropsy of cardiac origin, pass into an almost prolonged disuse in the treatment of heart disease, but with an undeserved popularity in the treatment of tuberculosis, to return again at the end of the nineteenth century to its position as the one most valuable drug for the therapy of heart disease.

Further study of ebbs and flows in medicine would undoubtedly yield other interesting information. More important would be a better understanding of the causes of such ebbs and flows, leading to a better understanding of the mechanisms of disease and of its prevention and treatment.

FEMORAL-SHAFT FRACTURES TREATED BY MEDULLARY NAILING*

EDWIN F. CAVE, M.D.†

BOSTON

AMERICAN orthopedic surgeons have been skeptical about the use of medullary nailing of long-bone fractures. This, I think, is fortunate, as the slow acceptance of this technic has allowed us to avoid many pitfalls that would have discouraged us as surgeons and would have led to abandonment of a procedure that is one of the great advances in fracture treatment during this century.

Medullary nailing of long-bone fractures is not a new procedure. It was used in ancient times in severe compound fractures. Nicolaysen in 1897[1] proposed such a form of treatment and Hey-Groves[2] in 1921 advocated the use of "a long steel strut" in badly comminuted fractures. However, because of the poor quality of metal available the method was abandoned, and it required the courage of Kuntscher,[3] a German surgeon, to show that the method was sound and that the medullary canal could tolerate a large cylinder of steel occupying nearly its entire diameter and still allow the fracture to heal.

INDICATIONS

The indications for medullary nailing are "broad or narrow depending upon the skill and experience of the surgeon with this technique and the facilities at hand."[4] Many surgeons will continue to use the more orthodox methods of traction and plaster fixation or both and, at times, open reduction with plate-and-screw fixation, but in the hands of a skilled bone-and-joint surgeon who is familiar with the technic of medullary nailing it can be the method of choice. It is not indicated in recent fractures in young children. Otherwise, age is not a factor. Our youngest patient was fifteen and the eldest eighty-six years of age. We do not necessarily urge its use in all fresh femoral fractures in adults, but in delayed union or nonunion and in many pathologic fractures of the femur it is by far the best available means of treatment. We believe it should not be employed primarily in compound fractures. It is better to allow healing of the soft tissues and later, within a few days, to insert the nail. It can be used in femoral shortening or for correction of rotation or angulation deformity. It is a tremendous aid in management of a patient with associated severe abdominal or chest wounds or with extensive burns when external fixation is not possible — provided, of course, that the patient can tolerate the major operation required for insertion of the nail. Thus, the method may well play an important role in war or disaster surgery.

*Presented at the annual meeting of the New England Surgical Society, York Harbor, Maine, September 22, 1951.

†Associate in orthopedic surgery, Harvard Medical School; chief of Fracture Service, Massachusetts General Hospital.

The Nail

The nail (Fig. 1) is manufactured of 18–8Smo. stainless steel, in diameters from 7 to 11 mm. and in lengths from 14 to 17 inches. It is cloverleaf-

Figure 1. *Drawing of the Medullary Nail.*

shaped when viewed in cross section and is hollow so that it may be driven over a guide rod. It has torsional strength produced by curves in both sides of the basic "U" design. The apex of the design has a well-rounded curve to induce strength, and the "eye" for extraction should be at least the diameter of the nail from the end.[5]

Technic of Inserting the Nail

Under general or spinal anesthesia, the patient lies on the side opposite to that of the fracture (Fig. 2). The injured jeg is prepared and draped so that both hip and knee can be flexed to as much as 90°. The incision can be placed posterolaterally, directly laterally or anterolaterally. The author's preference is for the anterolateral incision between

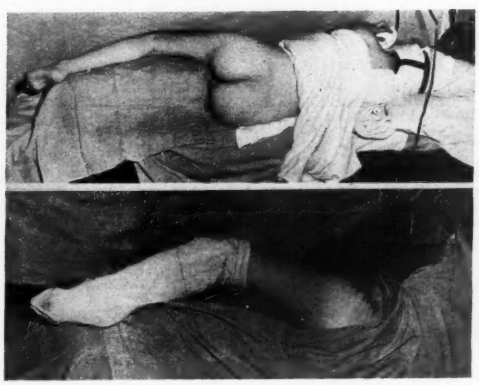

Figure 2. *Position for Insertion of the Medullary Nail.*

the rectus and the vastus lateralis muscles for the distal two thirds and the posterolateral incision between the vastus lateralis and the hamstrings for the proximal one third of the shaft. The fracture is exposed subperiosteally, sufficiently to mobilize both fragments and bring them up onto the wound. If the fracture is recent, it will probably be unnecessary to enlarge the medullary canal. If, on the other hand, nonunion has existed for some time, it will be necessary to enlarge the medullary cavity with a reamer or with gouges. The diameter of the canal is estimated by gently inserting a medullary nail that appears to be of the proper size. This should be done in both proximal and distal fragments. A guide rod of known length is then inserted into the proximal fragment (Fig. 3); it makes

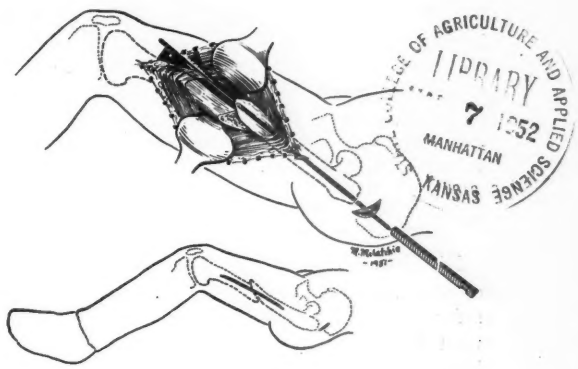

Figure 3.

its exit through the greater trochanter and becomes superficial under the skin, where a stab incision is made. The guide rod is driven out through this incision, and over the guide rod is fitted a medullary

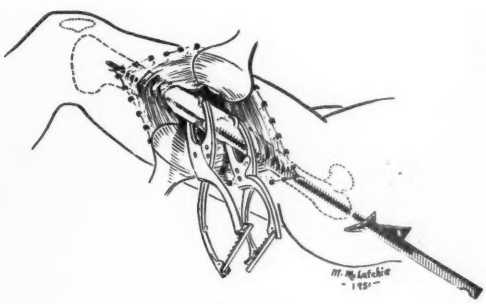

Figure 4.

nail of chosen size. This is driven about 1 inch into the bone. The guide rod is then withdrawn from the proximal fragment, reinserted superiorly into the hollow nail and driven down to the fracture line (Fig. 4). The fracture is reduced and held with clamps and the guide rod further inserted well into the distal fragment. Portable anteroposterior and lateral x-ray films are taken, to include the fracture site and the knee joint. Accurate measurement of the amount of guide rod in the femoral shaft can then be determined and a nail of proper length chosen. The medullary nail is then driven over the

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guide rod by gently tapping from above downward. If impingement is encountered one must proceed with great care, and it may be necessary to use a nail of smaller diameter. As the nail will not bend, one must eliminate the anterior bow of the femur by straightening the bone at the fracture site as the nail is driven into the distal fragment. Caution should also be exercised to avoid comminuting the fracture. Ideally, the nail should extend from approximately 1 inch above the greater trochanter to the level of the adductor tubercle distally. If a nail of proper size has been chosen and the fracture accurately reduced, good stability will be obtained. As a rule, it is unnecessary to use splint or plaster fixation after operation.

Postoperative Care

Muscle-setting exercises are started the day after operation and knee motion encouraged. When soft-tissue wound reaction has subsided, the patient is allowed to be ambulatory with crutches, bearing 50 per cent of his weight on the treated leg. The use of crutches is continued until muscular strength and gait are satisfactory and the surgeon is satisfied that the fracture is well stabilized.

Removal of the Nail

Generally speaking, the nail should be left in place for at least one year. In our series we have removed only two nails, one in a boy of eighteen at the end of one year and the other in a man of sixty-eight at the end of eighteen months. There was no reaction about either nail, and they could have been left in without harm.

Healing of the Fracture

The fracture apparently heals by extramedullary and periosteal callus. The impaction gained by weight bearing is an advantage and contributes to earlier union more than does any other known method.

Our personal experience with this method of treatment has been confined to 43 cases, 37 of which have involved the femur. Of the femoral cases, 22 of the fractures were traumatic in origin, 10 were fractures through a malignant process, 4 were in Paget's disease in the femur and 1 was a fracture due to extreme malnutrition.

Traumatic Cases

In the 22 cases due to trauma, the duration of the fracture ranged from one day to five years. Only 8 were classed as recent — under three weeks.

Case 1 (732226) (Fig. 5). H. S., a 20-year-old man, sustained a comminuted, oblique, simple fracture of the midshaft of the left femur on March 23, 1951, when the body of an automobile fell on him as he was working under it. Operation was performed three days later, with retrograde insertion of a medullary nail and an iliac bone graft. He was ambulatory in a walker 9 days after the operation. Excellent

Figure 5. *Preoperative Lateral and Anteroposterior Views in Suspension Splint.*

stability was obtained, and union progressed. Crutches were discarded on June 1, 1951, 2 months after operation (Fig. 6).

Case 2 (743835). J. S., a 15-year-old boy, was injured on shipboard on July 9, 1951, when he fell 50 feet from a mast, fracturing the right femur, right tibia and fibula. The tibia and fibula were treated by closed reduction and a Kirschner wire was put through the tibia for femoral traction. On July 21, a Kuntscher nail and Parham bands were inserted. Convalescence was uneventful. Ambulation was delayed because of the fractures of the tibia and fibula.

Seven cases had persisted for as long as six months:

Case 3 (1628613 — United States Army, Murphy General Hospital) (Fig. 7). G. D., a 24-year-old soldier, sustained a simple fracture of the shaft of the right femur in a motorcycle accident on August 8, 1948. He was placed in balanced skeletal traction for 1 week. On August 15 an open reduction with application of plate and screws was performed. The patient was in hip spica for 3 months, in skeletal skin traction for 3 months and ambulatory in a brace for 6 weeks. He returned to military duty on May 7, 1949, 9 months after the accident. He later had pain in the right knee and limped; he returned to the hospital in August, 1949. X-ray films then showed that the plate had broken and that there was considerable angulation of the femur at the fracture site. Examination revealed anterolateral bowing of the right thigh, with 1½ inches' shortening of the right leg. On September 15, through the same incision, the plate and screws were re-

moved, the medullary canal opened above and below and a Kuntscher nail inserted retrograde. The leg was supported in a Hodgen splint for 2 weeks, after which the patient was ambulatory with crutches. Eight months afterwards, the

FIGURE 6.

patient writes: "The rod doesn't bother me, but the knee gets tired and I still have a limp. I wear a ¾-inch lift. . . . They wanted to take the rod out, but I asked them to leave it in."

Two cases were of five years' duration; both were compound war wounds, and both had been previously infected and subjected to numerous bone-grafting procedures.

RESULTS

The results of nailing in this group have been most gratifying. All injuries have united by bone except one, an Army case in which nonunion and sepsis had existed for five years, later requiring amputation. Healing was satisfactory in the other five-year case.

CASE 4 (RA 35744161 — United States Army, Murphy General Hospital). P. B., a 26-year-old soldier, sustained a compound comminuted fracture of the upper third of the left femur from shrapnel on November 26, 1944, followed by infection and drainage and extensive bone loss. On April 23, 1946, plating and bone grafting were carried out. The plate was removed in June, 1946, because of infection. On July 3, 1947, a dual onlay graft was carried out, but this failed. On November 14, 1949, a Kuntscher nail was inserted. Postoperatively the patient was on penicillin and Chloromycetin. Although local inflammation developed, there was no drainage. On September 11, 1950, a report from Walter Reed General Hospital stated: "Patient discharged 1 month ago (10 months after insertion of rod) and he has no symptoms referable to the fracture site. We had considered re-inforcement with iliac bone but felt that it might be well to give him a trial at function for a longer period." As impaction of the fracture occurred, the nail projected into the knee joint. On May 22, 1951, the rod was extracted without difficulty and shortened by 1 inch. It was reinserted after rotating it 90° to give it a firm grip. The femur appears to be united, and the patient is walking without crutches with a high sole and a 3½-inch heel.

Many of these femur injuries have presented difficult problems and, in our opinion, could not have been handled effectively by any other known method. They have served as an excellent test of this means of treatment.

COMPLICATIONS

Complications in this group have been surprisingly few. Sepsis occurred in one case that had been previously plated and grafted. This, however, has subsided and a local sequestrectomy has been performed. The nail is still in place and the patient is at work in an office. Two patients developed

FIGURE 7.

localized phlebitis of the thigh, requiring anticoagulant therapy, but both recovered in three weeks and their convalescence was not delayed. There were no fat emboli. In this group we have been fortunate, as so many complications are possible in such cases. In the 700 cases presented in a symposium on medullary nailing (Chicago,[6] January, 1951), the complications that may follow this form of treatment were emphasized more forcibly than any other phase of the subject, in the hope that surgeons inexperienced in this technic would appreciate its dangers.

In these 700 cases, reported by 15 surgeons from all parts of the United States, the commonest complications were surgical shock, pulmonary emboli and infection. Fat emboli did not occur in a single

case. Infection occurred in 20 cases; 2 of these patients developed chronic osteomyelitis and nonunion resulted. In the majority of cases, however, the infection was transient and subsided after wound drainage and antibiotic administration. In no case was the pin removed because of infection.

Errors in technic were numerous. The important ones were: lack of proper preoperative planning; lack of proper instruments; breaking or bending of the nail during or after its insertion; splitting of the shaft or comminution of the fracture as the nail was driven in; improper length or diameter of the nail; poor reduction of the fracture; and impingement of the nail against the anterior cortex of the femur, making extraction difficult.

Pathologic Fractures

The nail has been employed by us in a total of 14 pathologic femoral fractures, with the following diagnoses: melanotic sarcoma, 1; metastatic carcinoma of the lung, 2; metastatic carcinoma of the prostate, 1; multiple myeloma, 3; malignant lymphoma, 1 patient with a pathologic fracture in each femur; osteoporosis from malnutrition, 1; Paget's disease, 3; and Paget's disease with nonunion, 1 — a total of 14 injured femurs in 13 patients.[7]

All patients were bedridden when the rod was introduced and would have remained so had not this form of stabilization been used, as in the following cases:

Case 5 (685851) (Fig. 8). G. R., a 56-year-old man, whose primary disease was malignant lymphoma, fell downstairs at home, sustaining fractures through metastatic areas in the left humerus and through the midshafts of both femurs on September 9, 1950. The fracture of the humerus was treated by supportive measures, and the femoral fractures were stabilized with Kuntscher nails on April 11, 1951, on the left and on April 17 on the right. Good stability was obtained. The patient was ambulatory in a walker 3 weeks after introduction of the second rod. He was discharged home approximately 1 month after the second operation. He died six months after the operation but was ambulatory with crutches and in no pain during that time.

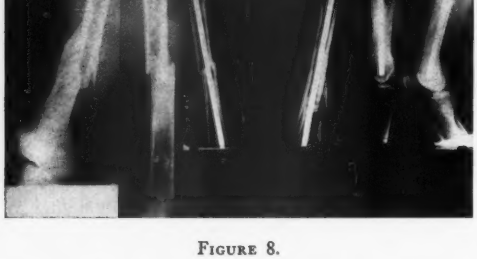

Figure 8.

Paget's disease is one of the conditions in which the use of the rod is most effective. We are taught that Paget's disease always heals. One of our cases, however, was ununited at the end of four months of skeletal traction.

Case 6 (677262) (Fig. 8). F. F., a 65-year-old man, whose primary condition was Paget's disease of both femurs, sustained a fracture through the lower portion of the right femur when he fell 4 months prior to admission in May, 1949. He was treated in another hospital with skeletal traction for 4 months, but union did not result. Treatment at this hospital consisted of open reduction and retrograde introduction of the Kuntscher nail in September, 1949, with the addition of rib bone. The patient was ambulatory 10 days after operation. Union has progressed satisfactorily. He walks well with a cane and has no pain. The rod migrated upward 3 months after its introduction, and it was necessary to reinsert it well into the cancellous bone of the femoral condyles. No further migration has occurred.

In the other 3 cases of osteitis deformans the use of the nail has also been followed by successful results.

Case 7 (683511). H. M., an 83-year-old man, whose primary condition was Paget's disease of both femurs and the pelvis, sustained a fracture of the midshaft of the left femur on November 14, 1949, when he fell while walking upstairs. Two days later, the fracture was stabilized by open reduction and retrograde introduction of the Kuntscher nail. Because of the marked bowing of the femur it was necessary to osteotomize the bone approximately 4 inches above the fracture site in order to introduce the nail into the distal fragment. The femur was shaped to the nail. Good stabilization and union were obtained. The patient is now ambulatory with a cane and has no pain (Fig. 9).

Figure 9.

Summary

A description of medullary nailing of femoral fractures has been given, with discussion of its indications and possible hazards. When this method is used by well trained surgeons in the proper surroundings and with adequate tools, it is without question a valuable means of handling many difficult femoral fractures.

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CHRONIC PYELONEPHRITIS SIMULATING ADRENOCORTICAL INSUFFICIENCY*

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THE clinical picture of a shock-like state presenting signs and symptoms indistinguishable from those of adrenal insufficiency may occur in patients with chronic renal disease with normal adrenal glands. This was first noted by Thorn, Koepf and Clinton in 1944[1] and by Sawyer and Solez in 1949.[2] The former group had observed 2 cases, the latter 1. This report is the third to appear in the literature and represents the fourth such case.

This particular entity, named "salt-losing nephritis" by Thorn, is not to be confused with nephritis coexisting with adrenal cortical insufficiency.[3] It must also be appreciated that Addison's disease may produce signs and symptoms of renal insufficiency; it was this fact that led to delay in diagnosis in all the reported cases. However, as in Addison's disease, the loss of sodium contributes primarily to the patient's morbidity and is probably the most important factor leading to his death. As a matter of fact, the two diseases seem to differ only in pathogenesis, renal tubular failure being common in both. In Addison's disease, insufficiency of adrenal hormone is the cause of this failure; in the case presented herewith the cause was inability of the tubules to respond adequately to a sufficient amount of hormone.

CASE REPORT

CASE 1 (80800). M. C., a 37-year-old woman, was first admitted to St. Barnabas Hospital on July 6, 1949, complaining of loss of weight, vomiting and weakness. The patient's general health and strength had always been good. The past history was noncontributory. A brother had died 5 years previously of Bright's disease, and her father had died 12 years ago of some type of "kidney ailment."

The history of the present illness dated back 2 months to May, 1949, when the patient noticed marked weakness. She consulted her family physician, who said that she had anemia. She was given liver injections and iron by mouth. Progressive loss of weight and the onset of vomiting caused her to consult a gastroenterologist, who reported a negative examination. However, the weakness and vomiting continued. Because of the possibility of gastric neoplasm undisclosed by x-ray she was sent to a surgeon, who admitted her to this hospital. Laboratory examination on admission revealed a blood urea nitrogen of 168 mg. per 100 cc. The patient was therefore referred for study.

Examination revealed a chronically ill, apprehensive woman in a state of collapse. The blood pressure was 98/60; the pulse was 110 and was weak and thready. The eye grounds were normal, except for a slight increase in tortuosity of the arterioles. The tongue was dry. The skin had lost its normal turgor. The remainder of the physical examination was negative.

Laboratory examination of the urine revealed a specific gravity of 1.007, with no albumin, no sugar and no important formed elements. The blood count showed a mild anemia, with a red-cell count of 3,640,000 and a hemoglobin of 10.3 gm. (63 per cent). The white-cell count was normal. The blood urea nitrogen was 168 mg., the nonprotein nitrogen 296 mg., the blood creatinine 10 mg. and the blood sugar 119 mg. per 100 cc. A phenolsulfonphthalein-excretion test revealed 2½ per cent of the dye returned after 2 hours. The patient's urinary output was adequate. A marked diminution of the blood volume was noted, with a deficit of more than 50 per cent of the total. There was also a moderate increase in the total serum protein, the figure being 8.6 mg. per 100 cc., representing marked hemoconcentration.

During the 2-day period of preliminary study, the patient's condition rapidly worsened, and she was placed on the "critical list." She continued to vomit everything taken by mouth and was maintained by intravenous feeding. In spite of this, however, there was no relief from the marked dehydration. At this point it was thought that the patient probably had Addison's disease or at least marked adrenal cortical hypofunction. Accordingly, 1 cc. of Eschatin (whole adrenal cortical substance) was given every 6 hours. The patient was also given enteric-coated tablets of 1 gm. of sodium chloride every 4 hours. There was an immediate and dramatic improvement of the patient's general status. She was placed on a diet of high-salt food, which she retained completely. She was still weak but was no longer prostrated. She received a total of 3 cc. of adrenal cortical extract, 4 cc. of desoxycorticosterone acetate (DOCA) and 3 tablets of DOCA daily. Unfortunately, the blood and urine chlorides were studied only after specific therapy had been instituted and were therefore found to be within normal limits. In spite of this it was thought that the following criteria for a diagnosis of Addison's disease had been satisfied: weakness, hypotension, loss of weight, gastrointestinal irritability, mild anemia, nitrogenous retention, small heart size by x-ray and therapeutic response to adrenal cortical hormone. She progressed very well on this therapy; after 3 weeks in the hospital the blood urea nitrogen was 78 mg. per 100 cc. and the creatinine had decreased to 6.7 mg. per 100 cc.

When the patient was no longer considered critically ill, confirmatory tests of adrenal insufficiency were attempted. A Kepler–Power water test was performed, but the patient promptly vomited the large volume of water required. The test was attempted again at a later date, with unsatisfactory results. On one occasion the urinary chloride excretion was found to be 21.6 gm. in 24 hours, with a total output of 2400 cc. The blood calcium was 12.8 mg. per 100 cc. An electrocardiogram revealed high T waves in leads I and II, suggestive of hyperpotassemia. An x-ray film of the chest showed the heart to be smaller than normal in proportion to the chest size and the size of the patient. She was therefore discharged on August 28, 1949 on a maintenance dose of desoxycorticosterone, 2 cc. twice a day, and Eschatin, 3 cc. daily. She did relatively well for the next month but then began to complain of a choking sensation, paresthesias, pain in the legs, marked irritability and nervousness. The blood pressure at this time was noted to be 120/80, the weight 169 pounds and the hemoglobin 12.5 gm.

The patient was therefore readmitted on September 18, 1949, for further evaluation. It had been noted that in spite

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of the excellent response to adrenal cortical substances early in the treatment her response had recently been less good. It was now suspected that the diagnosis of Addison's disease was in error and that the patient was probably suffering from renal insufficiency of an unusual type. Accordingly, further studies were made. The 6-hour glucose-tolerance test revealed blood sugars of 173, 200, 158, 150, 108, 100 and 100 mg. per 100 cc., certainly not characteristic of adrenal cortical insufficiency. The carbon-dioxide combining power was 7.7 and 9.1 milliequiv. per liter. The hematocrit revealed 30 per cent cells on one occasion and 26 per cent cells on another. A Fishberg concentration test revealed a fixed specific gravity of 1.008. Blood-volume studies showed about 45 per cent of the total expected normal blood volume. The electrocardiogram revealed markedly high T waves in all leads, evidence of hyperkalemia. Urinalysis revealed on one occasion 8 to 10 white cells and 2 to 6 red cells per high-power field — the only time that this abnormality appeared. The hemoglobin varied between 7.5 and 10.3 gm. per 100 cc. The nonprotein nitrogen was 420 mg. per 100 cc. The urea nitrogen ranged between 176 and 165 mg. per 100 cc. The whole or plasma blood chloride varied from 460 to 500 mg. and the blood creatinine was 11.5 mg. per 100 cc. The amount of 17-ketosteroids excreted in the urine was 12.4 mg. per 24 hours. A urea clearance revealed 9.1 per cent of normal. A repeated blood calcium was 12 mg. per 100 cc. A Thorn test was performed, employing 25 mg. of ACTH injected intramuscularly. This showed a normal eosinophil response. During this admission the patient was deprived of salt for several days at a time in an attempt at more adequate testing. During one such episode she was found in collapse, with a blood pressure of 54/30. She showed an immediate dramatic response to 1000 cc. of 5 per cent glucose in normal saline solution and 5 mg. of Cortate (desoxycorticosterone acetate) given intramuscularly. Despite this, the laboratory and clinical data sufficiently ruled out adrenal cortical hypofunction and more firmly established the presence of some unusual type of renal insufficiency simulating Addison's disease. The patient was accordingly discharged from the hospital and maintained on a high-salt diet without adrenal hormones.

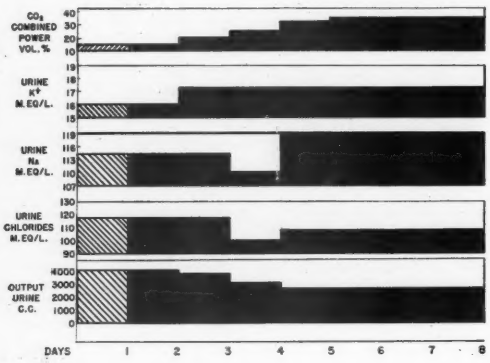

FIGURE 1. *Effect of Sodium Acetate in Renal Insufficiency.*

She returned to the hospital on January 13, 1950, complaining of general weakness. At this time the blood pressure was 98/68; the nonprotein nitrogen was 276 mg., the urea nitrogen 103 mg., the creatinine 13.7 mg. and the blood chloride 540 mg. per 100 cc. The urine chloride was 9.5 gm. in 24 hours on one occasion and 5.1 gm. in 24 hours on another. The blood calcium was 7.7 mg. per 100 cc. The patient was given daily intravenous injections of glucose in saline infusions, with marked clinical response.

For the next 8 months she was maintained on frequent transfusions (because of marked anemia), occasional infusions of glucose in saline solution, frequent calcium-gluconate injections, calcium lactate (orally) and as much as 12 gm. daily of enteric-coated salt tablets. On this regimen she complained of severe pains in the extremities, which were immediately relieved by intravenously given calcium gluconate, and of frequent episodes of severe vomiting. The blood pressure was maintained at about 120/80.

With the advent of cortisone, this therapy was instituted, but, as was expected, this did not alter the course of the disease.

Because of severe acidosis, hydrous sodium acetate (13.6 per cent) was administered in doses of 105 cc. daily, with a resultant increase in carbon-dioxide combining power to 16.4 milliequiv. (Fig. 1). In spite of this moderate alleviation of the severe acidosis, there was no alteration of the symptomatology. At this time the patient became severely depressed, in sharp contrast to the marked euphoria shown during the administration of cortisone. This depression progressed to a hysterical fear of impending death. She died suddenly on September 27, 1950 — a little more than a year after the onset of the illness.

Post-mortem examination revealed moderate pitting edema of both ankles. Although the external genitalia were essentially female, the hair distribution was suggestive of the male type. The heart was small in size, weighing 300 gm.; the ventricles contracted in systole. The lungs, liver, spleen, pancreas and gastrointestinal tract were normal. The right kidney weighed 80 gm., the left 110 gm. Both capsules were considerably adherent to the cortex, which on cut section appeared to be remarkably reduced in caliber; the left kidney contained a small cyst filled with clear fluid. Neither of the pelves was distended; dependent drainage was apparently good. The bladder was empty. However, a thick mucoid pus appeared to lie in pools in the mucosal folds. The mucosa was considerably congested and displayed several small bleeding points. The brain and pituitary gland appeared normal. The left adrenal gland contained a small cortical adenoma but was otherwise normal.

Microscopical examination of sections of the bladder showed much of the mucosa to be degenerated and replaced by hemorrhagic débris and inflammatory cells. These inflammatory cells were lymphocytes, eosinophils, neutrophils and macrophages. In addition there was a moderate amount of interstitial edema, which extended down to the muscularis of the bladder wall. Multiple sections of the kidneys showed marked distortion of the architecture. There was marked increase in interstitial fibrous connective tissue; in many areas this presented a moderately intense inflammatory infiltration composed principally of lymphocytes and plasma cells. However, in one area near the pelvis this inflammatory reaction appeared to be of a suppurative type, with the inflammatory cells being chiefly polymorphonuclear neutrophils and eosinophils. A few of the tubules showed evidence of active pyelonephritis, being filled with pus. In addition, there were areas of frank abscess formation. Many of the glomeruli showed various stages of degeneration. A moderate number of normal-appearing glomerular tufts showed concentric periglomerular fibrosis. The afferent arterioles showed marked hyaline thickening, with consequent narrowing of the lumens. Some of these arterioles presented lumens that were almost completely obliterated. The arteries showed an increase of connective tissue in the intima, which appeared to be dense and acidophilic. There was some reduplication of the internal elastic membrane and hypertrophy of the media. The tubules seen showed two types of pathologic alteration. Some were markedly hypertrophic and appeared dilated; these were in the regions of the normal-appearing glomeruli. Many appeared atrophic, cystic and distorted, being compressed by the increase in interstitial fibrous connective tissue. Rare tubules showed colloid casts within their lumens and were lined by atrophic flattened epithelium. These changes were more pronounced in the numerous scarred areas. The over-all picture in the kidney was one of long-standing chronic healed pyelonephritis, with recurrent acute pyelonephritis and pyelitis.

The sections of the adrenal gland showed normal architecture of the cortex and medulla. In one area there was a small circumscribed but not encapsulated cortical adenoma appearing architecturally in the zona reticularis.

Discussion

The clinical course of this case in nearly all details closely parallels the previously reported cases. The patient was a relatively young person with no known history of renal disease. The onset was indistinguishable from adrenal cortical insufficiency, and the response to specific therapy was dramatic. There was no reason to suspect primary renal disease except, perhaps, that there was greater nitrogenous retention than might be expected with pure adrenal disease. The urine was normal except for a low specific gravity. There was no albuminuria and no formed elements. In spite of the marked polyuria there was a markedly elevated blood nitrogen. As in Thorn's cases, the small heart, the hypotension, the normal eye grounds and the weight loss, nausea and vomiting were further convincing evidence of adrenal disease. In addition to this, adrenocortical hormone, desoxycorticosterone and salt dramatically relieved all the major complaints, including weakness, vomiting and vascular collapse. However, there was no major change in the blood chemistry, and it was because of this lack of response, despite prolonged hormonal therapy, that the true condition was finally suspected.

Observations over a period of time were then possible. Tests were performed to determine the amount of adrenal involvement in the total picture. A Thorn test with ACTH revealed normal suppression of eosinophils. The 17-ketosteroids were normal. A glucose-tolerance test was normal. This in itself must be considered an important differential diagnostic point, as in Addison's disease a hypoglycemic picture is typical, whereas in salt-losing nephritis a normal blood sugar is found.

The Kepler–Power test was attempted on several occasions, but the patient vomited the relatively large amount of water required. Furthermore, this test would have had no significance in this case, as the altered water excretion due to renal disease *per se* would render it valueless. It should be pointed out that in such cases with possible renal involvement a trial without desoxycorticosterone should be carried out while the patient is receiving an adequate amount of sodium chloride so that clinical evaluation for the need of DOCA may be established; even more revealing would be elimination of the sodium chloride and continuance of the DOCA.

Although it was considered that adrenal cortical insufficiency had no part in the patient's illness, it was decided to observe the effects of cortisone on the kidney and electrolytes. The patient had been ill for about one year with no great alteration in the clinical course, and it was hoped that some degree of chloride retention would be obtained. Thorn believes that the specific disturbance in "salt-losing nephritis" is the inability of the tubules to reabsorb chlorides due to an inadequate response to adrenal cortical hormone. Because of this, we did not expect cortisone to be effective. The marked elevation of the patient's morale, characteristic of cortisone therapy, was the only beneficial effect.

Persistent vomiting, relieved only by intravenously given saline solutions, was the most disturbing feature throughout the patient's illness. It was thought that this was due to the extreme unremitting acidosis. In an attempt to alleviate this, sodium acetate solution was given. The response of the serum bicarbonate, as measured by the carbon-dioxide combining power, was impressive. In five days it rose from 6.4 milliequiv. to 16.4 milliequiv. per liter (Fig. 1). In spite of this, however, there was a marked deterioration in the patient's general condition. She became much depressed and suddenly, with no other associated symptoms or signs, suffered cardiac standstill and died, with no preceding shock-like state, pulmonary edema, or any hint that death was near.

This type of clinical deterioration in the face of an improved blood pH has its basis in known physiologic concepts. The patient had an elevated blood potassium for months and then, without any further alteration of this level, died a "potassium" death. In fact, the potassium was a little lower at the time of death, only the pH of the blood having changed. This change in pH was due to the production of potassium bicarbonate. Thatcher and Radike,[4] in their studies on potassium intoxication in the albino rat, found no significant difference in the toxicity of potassium chloride, potassium acetate and potassium citrate. However, they did find that potassium bicarbonate caused death in their laboratory animal much sooner than any of the previously employed potassium salts. Fenn[5] explains the phenomenon by postulating that potassium bicarbonate is an alkalinizing salt and that K^+ and OH^- are synergistic in their physiologic reactions.

The development of the severe depression, however, is not only a result of the synergistic action of K^+ and OH^- ions but also a response to discontinuance of therapy with DOCA or cortisone. The explanation may be found in the work of Truszkowski and Duszynska,[6] who showed that both whole adrenal extract and DOCA protected normal mice against potassium poisoning but adrenalectomized animals were highly susceptible to the potassium ion. The patient apparently tolerated the higher levels of potassium ion under increased adrenal-hormone influence, but withdrawal of therapy made the potassium ion more toxic to the patient.

In Addison's disease the specific metabolic defect is the failure of tubular reabsorption of Na^+ and Cl^- and retention of K^+; in renal insufficiency of the salt-losing type, most, but not all, tubular metabolic functions are altered. Noteworthy is the fact that there was never any glycosuria in this case; this indicates that some threshold function remained in the tubules. Urea was reabsorbed un-

selectively, as is the case in lower-nephron nephrosis. Quite differently from lower-nephron nephrosis, however, there was a persistent marked polyuria. In spite of the polyuria, there was a persistent elevation in the level of the serum potassium. In renal insufficiency with an adequate urine volume, potassium retention does not characteristically occur.[7] It has been reported that potassium intoxication will not take place in the presence of polyuria. However, the physiologic antagonism of sodium and potassium is such that marked sodium depletion would tend to cause potassium retention. Hyperkalemia in these cases must also represent a reduced response of the tubular epithelium to desoxycorticosterone. Large doses of desoxycorticosterone did have a slight effect in this case, but it was obvious that large doses of sodium chloride were more important in maintaining electrolyte balance in this patient. Furthermore, reduced blood chlorides, which in themselves exercise a threshold function on excretion of chloride, do not necessarily always do so. Ambard[8] states that when the serum chloride falls below 96 milliequiv. per liter the excretion of urinary chloride ceases. This patient continued to excrete large volumes of chloride in spite of the blood chloride level of 78 milliequiv. per liter. Similarly, Peters[9] has maintained that chloride excretion cannot be forced beyond a certain fixed level in each case. However, in renal insufficiency of tubular origin chloride can apparently be excreted in large amounts in response to a large intake.

The severe, almost unremitting uremia found in this case has its explanation in several factors. First, there was renal insufficiency due to the intrinsic renal disease. Sufficient anatomic defect was demonstrable at post-mortem examination to account for this renal insufficiency. Secondly, depletion of sodium was an important factor. From this there followed the now well recognized "salt-depletion syndrome." This has been excellently described by Schroeder[10] and others as a major and often overlooked cause of uremia in the presence of renal disease.[11-13] Finally, diminished blood volume, which is characteristic of sodium depletion, has been shown to cause reduced glomerular blood flow. This will obviously result in nitrogenous retention.

During the course of her illness the patient complained frequently of marked weakness of the extremities. At one time she complained of "paralysis" of the lower extremities. This, of course, is not a paralysis in the true sense of the term but actually a myasthenic state, which has been described as occurring in association with Addison's disease, with its accompanying hyperkalemia and hyponatremia. McNaughton and Burchell[14] have recently described such a "myasthenic crisis" in association with a case of marked renal insufficiency with potassium intoxication. Their case was similar in many respects to the case here reported and can properly be so classified.

Finally, the underlying anatomicopathologic condition was revealed at autopsy as a chronic pyelonephritis — although there was no previous history of renal disease and, until terminally, no urinary or characteristic systemic findings. Weiss and Parker[15] and others[16, 17] have called attention to the insidious nature of chronic pyelonephritis; they state that it is the most frequent and most commonly overlooked type of progressive renal disease. Neither hypertension nor positive urinary or blood findings need be found at a single examination. The onset is usually masked and is often dismissed as insignificant, and the actual crippling effects on the kidney may be seen only many years later, either in the classically accepted form or in some ill-defined symptom complex.

Summary and Conclusions

A syndrome characterized by excessive loss of sodium chloride, resulting in Addisonian-type collapse and associated with renal rather than adrenal disease, is described. Thorn has termed this syndrome "salt-losing nephritis."

Although adrenocortical hormone is of no specific value in correcting the mineral depletion of these patients, because the renal tubular cell is unable to respond to hormonal influence, the hormone does play a part in enabling the patient to withstand higher levels of potassium ion than under ordinary circumstances.

Contrary to the reports of previous studies, it is possible that under certain conditions there is no minimum level of serum chloride below which excretion of urinary chloride ceases.

Hyperkalemia may occur in the presence of marked polyuria, probably dependent on marked sodium depletion.

High levels of serum potassium do not necessarily exert a toxic effect. Hormonal factors, the pH of the serum and the rapidity of their alteration are important in the production of toxicity.

Chronic pyelonephritis is a common disease, too often overlooked and deserving of consideration in ill-defined symptom complexes.

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THE GUILLAIN-BARRÉ SYNDROME: REPORT OF A CASE TREATED WITH ACTH AND CORTISONE*

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THE syndrome of diffuse peripheral neuropathy associated with albuminocytologic dissociation in the spinal fluid has received considerable attention in both American and European literature. The great variety of descriptive terms applied to the condition, — infectious neuronitis, radiculomyelitis, polyneuritis with facial diplegia and acute febrile polyneuritis, to mention a few, — reflects the confusion about the nature and limits of the entity. Until our fundamental knowledge about the process increases, the confusion is probably less compounded by continuing to identify the syndrome by the names of Guillain and Barré.

Most authors agree, however, that usually after a respiratory or other type of infection some patients develop a symptom complex characterized by paresthesias, muscle pain and rapidly progressive motor weakness. Sensory changes are present but are overshadowed by motor symptoms. These are often alarming and may progress to flaccid paraplegia, bladder and bowel involvement, disturbances in swallowing and cardiac rhythm and respiratory paralysis. A distinctive elevation of the spinal-fluid protein without pleocytosis occurs in 80 per cent of cases. The process generally increases in severity and extent for two to six weeks. Twenty per cent of patients die during this phase, usually of respiratory paralysis.[1-3] If the patient can be nursed through the period of respiratory dysfunction, however, the condition is peculiarly benign, and despite extensive paralysis complete recovery is the rule. This is rarely rapid; it commonly requires months or years.

The pathology of this process has been the subject of several reports.[4-6] Recent work has emphasized edema of the nerve roots as a prominent change, with myelin degeneration and beading of the axones.[7] There are associated and probably secondary changes in the anterior horn cells and possibly mild changes in the brain stem and even the cerebral hemispheres. There is often perineuronal infiltration with lymphocytes and some vascular engorgement, but evidence of acute inflammation is not prominent. Aring[8] and, more recently, Scheinker[7] have concluded that the initial pathologic event is edema of the nerve roots as they leave the spinal canal. Expansion of the roots within their relatively inelastic dural sheaths or, in the case of the facial nerve, within the fallopian canal, produces axon compression and secondary disruption of function. It also produces a block to the filtering of the spinal fluid and a consequent rise in the protein content of the fluid in the lumbar sac.

The cause of this nerve-root edema remains obscure. In the past a specific virus[8] and hypothetical "toxins" were implicated. Recently, however, several authors have pointed to certain similarities of this process to rheumatic fever and other "allergic" diseases that follow infections.[6, 9] Favour has particularly emphasized the role of allergy in the production of this syndrome and has likened it to "a hive of the central nervous system."[10] Because ACTH and cortisone are known to suppress the manifestations of hypersensitivity,[11] we thought it would be reasonable to determine the effect of these agents in the Guillain–Barré syndrome.

Case Report

Case 1 (RBBH 10177). J. W., a 59-year-old railroad engineer's helper, had a respiratory infection 1 month prior to admission to the hospital but was otherwise well until 7 days before admission, when he noted aching and weakness in his calves. Two days later, when first examined, he complained of generalized weakness, severe pain in his legs and back and numbness in his hands and feet. Examination failed to show significant muscle weakness. His symptoms continued to worsen, and on the day before admission he had difficulty in urinating and defecating. The past history was negative except for mild osteoarthritis of the knees, which had been treated at this hospital one year previously. Physical examination on January 27, the day of admission, showed a moderately obese man with generalized objective muscle weakness, although motion was possible in all extremities. Tendon reflexes were absent except for weak biceps jerks bilaterally. Position sense was absent in the toes. Temperature, pulse, respirations and blood pressure were normal. Routine urinalysis, white-cell count, differential and hematocrit were normal, although the corrected sedimentation index was 1.1 mm. per minute. Blood and spinal-fluid Hinton tests were negative. Lumbar puncture showed normal pressure and dynamics, with one lymphocyte per cu. mm., and a protein content of 132 mg. per 100 cc. The colloidal gold-sol curve was 0001243211.

The patient was treated symptomatically and observed. On January 31 the pain had been replaced by numbness in

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the legs but was more severe in the arms and shoulders. He had difficulty in raising sputum, and his speech was thick and slurred. Neurologic examination showed for the first time a bilateral facial paresis, more marked on the right. The hands and arms, especially the triceps muscles, were weak, and except for slight motion of the toes the legs could not be moved. Position sense was absent in the toes and ankles, and there was diminished pin-prick and light-touch sensation over the feet. Deep tendon and superficial reflexes were absent except for the cremasteric reflexes, and there was complete bladder insensitivity and bowel paralysis.

On February 1 the patient was placed on ACTH. The eosinophil count fell from 210 to 61 per cu. mm. 4 hours after an initial dose of 35 mg. Neurologic examination 6 hours after the first dose showed a return of position sense in the left foot, slight but definite improvement in the strength of the arms and improvement in the voice. After 48 hours the voice was normal and the facial weakness had disappeared,

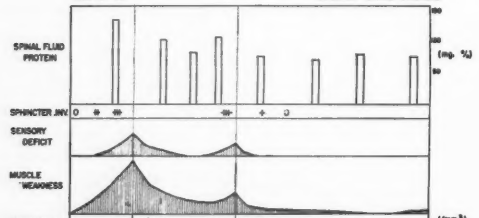

FIGURE 1. *Clinical and Laboratory Data on J. W.*

except for a slight deficit on the right. The patient was maintained on 40 mg. of ACTH a day, later increased to 80 mg. daily. Subsequent improvement was slower but, as measured by daily neurologic examinations, steady for 10 days. By the seventh day of therapy pain was almost absent, the legs could be moved freely and triceps jerks and abdominal reflexes had returned. The spinal-fluid protein fell to 100 mg. per 100 cc. on the 5th day and to 82 mg. per 100 cc. on the 9th day of treatment.

On February 12 it was noted that position sense was again absent in the toes of the right foot and that there was again some right-facial weakness. The spinal-fluid protein had risen to 104 mg. per 100 cc. on February 13. Concomitantly, the eosinophils, after an initial fall to 6 per cu. mm., had risen to 312 per cu. mm. on February 12 and to 467 per cu. mm. on February 14; a repeat ACTH test showed a decrease of only 17 per cent. The basal metabolic rate was found to be −4, and the eosinophil decrease after administration of adrenalin (0.3 mg., subcutaneously) was 42 per cent. It was thought, therefore, that the rise in the eosinophil count was due to adrenocortical unresponsiveness to the injected ACTH. Accordingly, on February 16 the patient was placed on intramuscularly given cortisone, 300 mg. per day. The eosinophil count again fell to 40 per cu. mm. on February 20 and to 19 per cu. mm. on February 24. The facial weakness promptly disappeared, position sense returned in the right foot and there was general improvement in muscle strength. After 36 hours of cortisone treatment the patient had his first normal bowel movement since the beginning of therapy, and he noted some return of bladder sensation. Improvement was again slower but uninterrupted. The spinal-fluid protein was 76 mg. on February 19, 69 mg. on February 26, 82 mg. on March 5 and 76 mg. per 100 cc. on March 13. The patient made a good clinical recovery, the muscle examination returned to normal and weak ankle and knee jerks reappeared. The objective sensory examination became normal, but a feeling of numbness in the hands, particularly the right, persisted. The patient also had the sensation of walking on pneumatic cushions, which gradually grew less marked. After a gradual decrease in dosage, cortisone was discontinued on March 12. Thereafter there was a slight recurrence of objective weakness in the right arm, but the patient felt well and was discharged on March 19.

He continued to improve subjectively, and his strength and endurance increased. On May 16, 1951, he underwent cholecystectomy for cholelithiasis and an acute cholecystitis. He made an uneventful convalescence from the operation. On July 19, when last seen, the patient looked well. He reported that he was running a rooming house but did not feel strong enough to return to work on the railroad. The strength of his extremities seemed normal on the usual tests. Objective sensory examination was negative. He still complained of a feeling that he was walking on a very thin cushion under the right foot. Tendon reflexes were normally active and equal in the arms. The knee and ankle jerks were elicited with reinforcement.

DISCUSSION

The results of steroid therapy in the present case must, of course, be interpreted with considerable caution, as the Guillain-Barré syndrome may vary greatly in its clinical course. We believe, however, that the reaction of this patient probably represents a specific therapeutic response, for several reasons. In the first place, although cases have been reported in which recovery was rapid,[12, 13] the course is usually prolonged. Brain states that "in the most favorable cases, the patient is not likely to be convalescent in less than three to six months."[1] The pretreatment course of this patient was ominous. In addition to a flaccid paraplegia, he showed early signs of respiratory involvement, difficulty in raising sputum and abdominal-muscle involvement. The latter signs are of grave prognostic import. Sphincter disturbances are also more common in fatal cases, since they occurred in 25 per cent of the autopsied cases reported by Haymaker and Kernohan,[4] whereas they are rare in nonfatal cases. Furthermore, the paralysis, once having reached its height, tends to remain stationary for some weeks before improvement begins. On the other hand, in the present case the steady downhill course was reversed and improvement was apparent several hours after treatment had been started. The clinical relapse that accompanied the development of adrenocortical unresponsiveness fortuitously presented the opportunity of repeating the experiment in a slightly different fashion. The relapse promptly disappeared with re-establishment of effective circulating glucocorticoid levels. Finally, the rise and fall of the spinal-fluid protein level paralleled the variations in the eosinophil counts and in the clinical course, points well shown in Figure 1. It is unusual for the protein level to fall so early in the course of the disease,[2, 4] and no previously reported therapy has brought about a lowering of this level.

The improvement in this case could reasonably be attributed to therapy, if one considers the syndrome to be a disease of hypersensitivity. In the past, a tendency to regard any case with diffuse neuritic involvement and an elevated spinal-fluid-protein content as an instance of the Guillain–Barré syndrome has led to much confusion. Some

of the reports undoubtedly deal with other entities. The complications of diphtheria and diabetes, and the encephalomyelitides complicating a variety of viral infections[6, 14-16] have been reported as cases of this syndrome. They are probably more properly regarded as specific entities that may present the clinical picture of extensive neuritis and albuminocytologic dissociation.[1, 17, 18]

When reports of this type are eliminated, however, there remains a group of patients in whom the only etiologic clue is a preceding bacterial infection. There is much to suggest that such cases represent an allergic or hyperergic response to bacterial infection. Cases are repeatedly reported as complications of such diseases as peritonsillar abscess,[9] pharyngitis, bronchitis, pneumonia, scarlet fever[16] and gastrointestinal disturbances.[19] The sequence of infection, latent period and symptoms is seen in the diseases of hypersensitivity. Furthermore, cases have been reported as following tetanus-antitoxin injection, and one such case developed while urticaria appeared on the skin.[1, 16] Other cases have been associated with serum sickness.[6] The erythrocyte-sedimentation rate is often elevated during the illness[4], and the antistreptolysin titer may also parallel the course of the process.[9] The reported pathologic picture is also consistent with an allergic etiology. The primary nerve-root edema lacks the characteristics of infectious inflammation and is not unlike the allergic edema seen in other organs in a variety of diseases.

If the underlying process were allergic, the adrenal steroids would be expected to bring about prompt resolution of the congestion and edema. Spinal-fluid drainage would improve, and the protein content would fall. The speed of clinical recovery, however, would depend on the degree of nerve injury. Brief periods of axon compression are consistent with prompt return of function on release of the compression, but repair of nerves damaged by more prolonged compression requires long periods of time.

This predicted response was observed in detail in the present case. In both the initial response and the recovery following the relapse, there was dramatic improvement of the newest lesions and a fall in the spinal-fluid protein. Later improvement was slower, and slight subjective changes persisted when cortisone was stopped.

Because this syndrome has a mortality of 20 per cent in spite of the most careful management and because it entails a prolonged, costly period of convalescence for those who survive, the value of an effective therapeutic agent is manifest. In the past, therapy has been mainly symptomatic and supportive in the active stage and designed to aid rehabilitation during convalescence. Favorable responses to x-ray therapy,[20] neostigmine[21, 22] and BAL[23-25] have been reported. The responses to irradiation and neostigmine, however, are probably nonspecific and temporary,[15, 20] and Nielsen's[23, 24] results with BAL require confirmation. Creaturo[26] used a proprietary adrenocortical extract as part of the supportive therapy, but no reports on results of ACTH or cortisone therapy during the early, progressive stage of the process are available.

These observations on a single case are reported because the syndrome is relatively uncommon. It is, of course, impossible to make any definite statement about the value of steroids in the management of this condition at present. The results, however, seem promising enough to justify further investigation.

It should be emphasized that if this hypothesis of the pathogenesis of this syndrome is valid, intensive glucocorticoid therapy in the early progressive stage of the process is necessary if measurable clinical improvement is to be obtained. Treatment of established cases would be expected to halt any further progression of the process and might lower the spinal-fluid protein, but there is no evidence that it would speed recovery of neurons damaged by prolonged compression.

Summary

A case of the Guillain–Barré syndrome treated with ACTH and cortisone is reported. The patient showed improvement on ACTH, relapsed when his adrenal glands became unresponsive to this agent and again improved on cortisone.

The response of this patient, in addition to other evidence, supports the hypothesis that some cases of the Guillain–Barré syndrome represent an allergic response of the nervous system to bacterial products. It is suggested that this reaction causes congestion and edema of the nerve roots, with secondary compression in their inelastic dural sheaths, and that adrenal steroids produce resorption of this edema and permit axon recovery, the speed of recovery depending on the duration of the compression.

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MEDICAL PROGRESS

A COMPARISON OF THE CLINICAL FEATURES OF POLIOMYELITIS IN ADULTS AND IN CHILDREN

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ONE of the remarkable changes that have occurred in poliomyelitis in many parts of the world in the past twenty years is the rise in its incidence in older age groups.[1] Formerly uncommon in others than the pre-school child, the disease has gradually become frequent in those five to nine years old and is, at present, increasing in prevalence in even older persons. As a matter of fact, it is not at all rare today for poliomyelitis to affect patients in the third and fourth decades of life. Because of this changing age frequency, the term "infantile paralysis" is no longer applicable to the clinical picture as a whole; this infection, which in the past was first observed and treated almost exclusively by the pediatrician, now comes in many cases to the attention of the internist.

Poliomyelitis in the adult is said to be accompanied more frequently by muscle pain and less often by a biphasic type of onset than in the child. It is also generally accepted that it is more severe and has a higher mortality rate in the older than in the younger age groups.[2] Studies in which all the clinical details of the infection in children and in adults have been compared and contrasted are not available, however. In 1949 the opportunity of observing a large number of persons of all age groups during a single "epidemic" season presented itself to the authors. The purpose of this report is to describe the clinical features of poliomyelitis in these patients and to point out certain differences that were probably related to age and on the basis of which the disease could be differentiated into "childhood" and "adult" types.

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METHODS

All poliomyelitis patients admitted to the Haynes Memorial Hospital from May through December, 1949, were included in the study. The diagnosis in each case was established on the basis of two or more of the following criteria: history of contact with a known case in or outside the patient's family, a suggestive prodrome, signs of meningeal irritation, spinal-fluid changes consistent with poliomyelitis and evidence of cranial-nerve, anterior-horn-cell or medullary dysfunction. In all cases of nonparalytic disease in which the possibility of mumps meningitis was suspected this infection was ruled out by determination of erythrocyte-agglutinin-inhibition titers in the acute and convalescent phase. Although it is possible that some of the nonparalytic group had Coxsackie-virus disease, no effort was made to rule out this disease because of the lack of necessary laboratory facilities.

After admission, complete physical examinations were carried out once or twice a week. Laboratory studies consisted of hemoglobin determination and white-cell count; urinalyses were carried out at least once a week. Spinal puncture was performed at the time of admission to the hospital; it was not

repeated unless the fluid was entirely normal when first studied or there was an unexplained change in the course of the illness. All patients, with or without paralysis, were evaluated at least once a week by an experienced physiotherapist and the degree of strength of all muscles was noted and recorded according to the standards of the National Foundation for Infantile Paralysis. One or more of the authors also made a complete survey of muscle function at least once weekly in every case.

Treatment of nonparalyzed patients consisted of ten days of bed rest and discharge from the hospital after four to five days of ambulation. For those with paralysis of the extremities bed and footboards were used routinely; graduated physiotherapy was initiated forty-eight hours after the temperature had returned to normal. Ambulation was permitted as soon as practicable. Hot wet packs and dry heat were employed regularly for relief of pain and so-called spasm. The tank respirator was used in all cases of paralysis of the diaphragm and chest muscles of a degree sufficient to embarrass respiration. The phrenic stimulator was applied only when involvement of the respiratory center was evident. When swallowing was impaired because of dysfunction of the 9th and 10th cranial nerves, gravity drainage and suction were employed. Tracheotomies were performed infrequently; they were carried out if the quantity of secretion was so great that suction and drainage were ineffective in maintaining a clear airway, if major recurrent atelectasis occurred or if bacterial pneumonia supervened and the patients were unable to cough up thick, purulent secretions. Bladder paralysis was managed by tidal drainage. No chemotherapy was given for the primary disease. Secondary bacterial infections were treated with antibiotics selected on the basis of the type of causative organism. Oxygen was administered to all patients who showed any respiratory difficulty.

All patients, with or without paralysis, were examined at least twice a week by a neurologist and at least once weekly by an orthopedist who evaluated the state of muscle function. All cases, regardless of the presence or absence of any type of paralysis, were referred to various out-patient orthopedic clinics, where they were usually seen by physicians who had cared for them during the period of hospitalization. The duration of the follow-up period varied according to the type and severity of the disease but was usually three to eighteen months or more.

Results

Four hundred and twenty-eight patients were studied. When the pertinent data were obtained, the cases were divided into four age groups, for the following reasons: The ages 0 to 5 represent the group in which poliomyelitis was once predominant; most of the descriptions of the disease in the modern textbooks of pediatrics and medicine are based on the clinical findings in such children. The limits six to fifteen years were selected because in some parts of the world this includes a large proportion of cases and because it is uncommon for persons over fifteen years of age to be seen by pediatricians. The patient of sixteen years or older is usually seen by a general practitioner or an internist at the beginning of an illness. Those patients of sixteen to fifty years were divided into two groups, sixteen to thirty and thirty-one to fifty, in order to determine whether any differences existed in the course of poliomyelitis in young and middle-aged adults.

Table 1. *Prodromal Manifestations of Poliomyelitis in 428 Patients by Age.*

Age	No. of Patients	Prodromal Manifestations				
		Upper-respiratory	Gastro-intestinal	"Grippe"	Upper-respiratory and gastrointestinal	None
yr.		%	%	%	%	%
0– 5	50	36.0	6.0	22.0	4.0	32.0
6–15	161	27.3	6.2	24.3	2.5	39.7
16–30	165	19.4	14.7	36.3	3.0	28.5
31–50	52	9.6	15.4	32.7	0	42.3

Fifty patients were between the ages of six days and five years; 161 were from six to fifteen years old; 165 were sixteen to thirty-one; and 52 were aged thirty-one to fifty. As used in this paper, the term "adult" refers to those sixteen years of age or over; "child" includes those between one week and fifteen years old; there were 211 in the younger and 217 in the older group. There was a moderate difference in sex incidence in relation to age; 50.6 per cent of the adults and 60.7 per cent of the children were male. Analyses of all cases of poliomyelitis in Massachusetts in 1949 revealed a slight preponderance of females in the adult group.[3]

Prodrome

The variations in the types of onset and clinical forms of poliomyelitis at different age levels are presented in Table 1. Prodromal manifestations of sore throat, fever and other complaints suggestive of an upper-respiratory infection were commonest

in the youngest patients and became less frequent with increasing age. Symptoms of a mild gastrointestinal upset prior to the appearance of signs of meningeal irritation, on the other hand, were at least twice as common in adults as in children. The "grippe" prodrome, — generalized aching and fever with no localizing signs, — occurred about 1½ times more often in adults. The oldest age group contained the largest percentage of patients in whom no prodrome preceded the development of central-nervous-system involvement.

Table 2. *Symptoms and Signs of Poliomyelitis in Various Age Groups.*

Symptom or Sign	Percentage of Patients by Age Group			
	0–5 yr.	6–15 yr.	16–30 yr.	31–50 yr.
	%	%	%	%
Stiff neck	46	84.4	88.5	90.4
Headache	38	79.5	85.0	90.4
Muscle pain	32	41.0	58.1	55.8
Sore throat	32	26.7	33.3	13.5
Chills	4	12.4	29.7	26.9
Difficulty in swallowing	6	20.5	17.0	19.5
Difficulty in urination	2	5.6	26.1	25.0
Irritability	26	6.9	3.2	3.8
Chest pain	0	1.9	4.2	5.8
Bladder paralysis	4	3.1	32.1	28.8
Lymphadenopathy	20	24.2	12.1	7.7
Gastrointestinal dysfunction	4	2.5	17.0	19.3
Cyanosis	2	2.5	10.9	13.5
Rash	2	1.9	7.3	38.5

Symptoms

Many symptoms noted by the patients or their relatives and described to the physicians at hospital admission showed no significant differences in incidence among the various age groups. These included, in the order of frequency: fever, 78 per cent; stiffness of back, 53 per cent; vomiting, 49.8 per cent; generalized weakness, 44.6 per cent; nausea, 44 per cent; anorexia, 42 per cent; constipation, 21 per cent; malaise, 20 per cent; nasal quality of voice, 11.5 per cent; dizziness, 8.2 per cent; hyperesthesia and paresthesias, 8.2 per cent; difficulty in breathing, 7.7 per cent; diplopia, 6.3 per cent; stiffness of legs, 4.0 per cent; and drowsiness, 1.6 per cent. The percentages refer to the entire group of 428 patients.

Some symptoms that varied in incidence among the different age groups are recorded in Table 2. Most striking were the following: Stiffness of the neck was noted almost twice as often by those between the ages of six and fifty as by the younger patients. Pharyngeal discomfort was least common in the older adults. Difficulty in urination was from 4 to 13 times greater in adults than in children. Diarrhea occurred twice as frequently in children up to five years old as in any of the other age groups. In analyzing such data, important consideration must be given to the inability or unwillingness of some patients, particularly the younger ones, to bring their complaints to the attention of a parent or physician. Although this reduces the over-all significance of these observations, it probably does not invalidate them, as certain symptoms that showed significant differences, such as difficulty in swallowing and inability to urinate, are sufficiently discomforting that they are reported by young patients or observed by the parents.

Several of the physical findings noted at the time of admission showed no significant variation with age. Omitting all types of paralyses, these included stiff neck (83 per cent), stiffness of the back (82.5 per cent), positive Kernig sign (38 per cent), inflammatory reaction in the pharynx (23 per cent), splenomegaly (0.9 per cent) and hyperesthesia (0.9 per cent). (The percentages refer to the entire group of 428 patients.) In Table 2 are listed the physical findings that varied in incidence in different age groups. Paralysis of the bladder was 7 to 10 times more common in adults than in children. Generalized lymphadenopathy was found in 20 per cent of the group five years of age or less and in only 12.1 to 7.7 per cent of those sixteen to thirty and thirty-one to fifty years old, respectively.

Table 3. *Clinical Types of Poliomyelitis in Various Age Groups.*

Clinical Type	Incidence in Entire Group	Percentage of Patients in Various Age Groups					
		0–5 yr.	6–15 yr.	average for children	16–30 yr.	31–50 yr.	average for adults
	%	%	%	%	%	%	%
Nonparalytic	28.0	26	36.7	34.0	23.0	19.2	22.3
Bulbar	10.5	4	14.9	11.0	8.5	9.6	8.9
Bulbospinal	16.3	4	16.8	13.8	21.5	17.3	19.5
Spinal	45.0	66	32.3	41.2	47.3	53.8	48.9

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Severe gastrointestinal dysfunction, — marked meteorism, fecal impaction, partial paralytic ileus or moderate to severe generalized abdominal pain, — was 5 to 8 times more frequent in adults. Cyanosis, a reflection of the severity of the disease, was 5 times more common in those over sixteen years of age than in children. It has frequently been stated that rashes are uncommon in poliomyelitis. This impression is probably due to the fact that most observations have been made in children. Skin eruptions were observed with increasing frequency at older ages; among patients thirty-one to fifty years old rashes were manifest approximately 19 times more frequently than among patients under fifteen years of age.

Distribution of Clinical Types of Poliomyelitis

When all patients were considered, the most common type of poliomyelitis was found to be that affecting, in varying degree, the spinal cord alone — 45 per cent. Bulbar and bulbospinal involvement occurred in 10.5 and 16.3 per cent of the cases respectively. The remainder, — 28 per cent, — had no paralysis, even in the follow-up period. No cases of unquestionable polioencephalitis were noted. When the various clinical forms of the infection were analyzed according to age distribution, some differences in incidence were apparent (Table 3). Thus, spinal paralysis was commonest in those up to five years old and least frequent in children aged six to fifteen; however, it was somewhat higher in adults than in children. The incidence of bulbar disease was approximately equal in children and adults. Bulbospinal involvement occurred in 13.8 per cent of the children and 19.5 per cent of the adults. Nonparalytic illness was observed most often in children. When all types of paralytic poliomyelitis (spinal and bulbar) were grouped together, the total incidence in children (0–15) was approximately 66 per cent and in adults (16–50) about 77 per cent. These data reveal, therefore, an insignificant difference in the incidence of paralysis in adults and children hospitalized for poliomyelitis.

TABLE 4. *Extent of Involvement in Spinal-Paralytic Poliomyelitis in 259 Patients.*

Muscles Involved	Percentage of Total Group	Percentage of Patients by Age Group			
		0–5 yr.	6–15 yr.	16–30 yr.	31–50 yr.
		%	%	%	%
One leg	22.8	54.3	16.9	18.7	17.1
One arm	18.1	14.3	27.3	14.3	14.3
Both legs and arms	17.4	0	9.1	26.8	22.8
Both legs	16.6	14.3	15.6	17.0	20.0
One arm and both legs	8.5	2.9	5.2	12.5	8.6
One arm and one leg	7.0	8.6	7.8	5.4	8.6
Both arms	6.6	2.9	10.4	5.4	5.7
Both arms and one leg	3.1	2.9	7.8	0	2.9
Diaphragm and chest	14.7	0	15.8	65.8	18.4
Abdomen	14.3	0	32.4	56.8	11.8
Back	12.7	5.8	27.3	54.6	11.8

Extent of Involvement in Cases of Spinal Paralysis

Two hundred and fifty-nine patients had either isolated spinal or bulbospinal poliomyelitis. Of these, 35 were five years old or less, 77 between six and fifteen, 112 between sixteen and thirty and 35 between thirty-one and fifty years of age. Analysis of the entire group, without respect to age, revealed that paralysis of one leg was most common, whereas involvement of one lower and both upper extremities was least frequent. When the degree of muscle dysfunction was examined from the standpoint of age distribution, some remarkable differences were noted (Table 4). Paralysis of one leg occurred most frequently in children five years old or less; it was only about 1/3 as high in incidence in any of the other age groups. Weakness of a single upper extremity was most common in those six to fifteen years old. Very striking was the marked difference in the incidence of quadriplegia. This

TABLE 5. *Type of Bulbar Poliomyelitis in 114 Patients.*

Types of Bulbar Involvement	Percentage of Bulbar and Bulbospinal Cases	Percentage of Patients by Age Group			
		0–5 yr.	6–15 yr.	16–30 yr.	31–50 yr.
		%	%	%	%
N III, IV and VI	21.9	0	17.6	31.1	14.3
N V	7.0	0	7.8	8.9	0
N VII	43.9	75	39.3	44.5	50
N VIII	0.9	0	0	2.2	0
N IX and X	78.0	75	78.4	80.0	72
N XI	9.6	0	11.8	11.0	0
N XII	6.1	0	7.8	6.6	0
Medulla	12.3	0	7.8	15.5	21

was not observed at all in the very young children and was 2.5 to 3 times more frequent in adults than in those aged six to fifteen. Paralyses of the diaphragm and abdominal, dorsal and intercostal muscles occurred 2 to 4 times more often in the patients sixteen to thirty years old than in the others. The two age extremes showed the lowest incidence of these types of involvement. These data indicate that, although there is only a small difference in the total incidence of spinal-paralytic poliomyelitis in hospitalized adults and children, the degree of involvement is considerably greater and more serious in the older age group. Most significant is the fact that the paralyses that may endanger life, — those of the diaphragm and chest muscles, — occurred with greatest frequency in young adults sixteen to thirty years of age.

Types of "Bulbar" Poliomyelitis

The incidence of bulbar involvement in the 428 patients studied was 21.3 per cent. This type of disease occurred least frequently in the young children (five years old and younger — 8 per cent) and in the following percentages in the other age groups; six to fifteen years, 31.62 per cent; sixteen to thirty years, 27.72 per cent; and thirty-one to fifty years, 26.88 per cent. The distribution of various types of bulbar poliomyelitis at different age levels is presented in Table 5. When all the bulbar cases were considered, it was found that involvement of the vagus and glossopharyngeal nerves was commonest and was followed in frequency by damage to the innervation of the ocular muscles. The eighth cranial nerve was the one least often affected. Medullary paralysis, mainly with dysfunction of the respiratory center, occurred in 12.3 per cent of all patients with bulbar disease.

TABLE 6. *Case-Fatality Rates in Various Age Groups.*

AGE	NO. OF PATIENTS	DEATHS	
yr.		NO. OF PATIENTS	PERCENTAGE OF PATIENTS
0– 5	50	0	0
6–15	161	2	1.3
16–30	165	14	8.6
31–50	52	4	7.7

Function of the third, fourth, fifth, sixth, eighth, eleventh and twelfth nerves and of the medulla was not disturbed in any of the children five years old or less. The incidence of paralysis of the fifth, ninth and tenth nerves in this group, — 75 per cent, — seems high because of the small number of cases that it included. The absence of involvement of the fifth, eighth, eleventh and twelfth cranial nerves in those thirty-one to fifty years of age is notable. Medullary paralysis increased with increasing age and was commonest in the older adults; this is of the greatest importance because of all the types of bulbar poliomyelitis this is the one that most endangers life. In each age group, the commonest difficulty was inability to swallow because of dysfunction of the ninth and tenth cranial nerves.

Case-Fatality Rates

A study of case-fatality rates (Table 6) produced striking evidence of a difference in severity of poliomyelitis in children and adults. Of 50 children five years old or less, none died. The largest number of deaths occurred in the adults — 8.6 per cent in those sixteen to thirty years old and 7.7 per cent in the group thirty-one to fifty years of age. When all children (fifteen years or less) were compared with all adults (sixteen to fifty years), the death rate in the older patients was seen to be approximately 9 times higher than in the younger ones.

TABLE 7. *Types of Paralysis in 20 Fatal Cases.*

TYPE OF PARALYSIS	PERCENTAGE OF CASES
Both arms and legs	68
One arm	10.5
Both legs	10.5
One arm and one leg	5.3
Both arms	5.3
Diaphragm	70
Chest muscles	55
Abdominal muscles	30
Back muscles	10
Urinary bladder	80
N IX and X	65
N VII	40
N III, IV and VI	20
N V	0
Medulla	90

Since both groups were large and approximately equal in number, this is a statistically significant difference.

Eighty-five per cent of those who died had bulbospinal disease; the spinal form was present in 10 per cent and bulbar involvement alone was found in only 5 per cent. Table 7 presents the other clinical findings in these cases.

Pregnancy

One of the problems in poliomyelitis, peculiar to the adult, is pregnancy. There is little doubt, from the evidence available in the literature,[4-7] that the gravid state is deleterious to the person invaded by the virus of poliomyelitis. Of all females between the ages of sixteen and fifty included in this study, 19 per cent were pregnant; the incidence of pregnancy in the married women in this group was 29 per cent. Thirty-one per cent of those sixteen to thirty years old and married were pregnant. As estimated from rates of living and still births in the Commonwealth of Massachusetts, approximately 7 per cent of all women in this age group would be pregnant at a given time. Thus, in the females of these ages admitted to the hospital with poliomyelitis, the incidence of pregnancy was at least 4 times higher than expectancy.

In addition to increasing susceptibility to poliomyelitis, in many cases pregnancy was found to alter the course of the infection. Women who developed the disease early in pregnancy and were well along in the convalescent phase at the time of delivery suffered no ill effects. If, on the other hand, parturition took place in the acute phase or shortly thereafter, there was frequently an increase in severity of the paralysis or an extension of the involvement to muscles previously unaffected.

Discussion

There is little doubt that poliomyelitis is becoming more common in older persons. Careful epidemiologic investigations in various parts of the world have revealed a gradual upward shift in age incidence during the past twenty years. This phenomenon is probably a reflection of the presence of strains of virus that are antigenically distinct from the Lansing strain, for which a large number of older children and adults have neutralizing antibodies in their serum. The absence of such protection against the newer viruses may explain the increasing incidence of the disease in older children and adults.

In this study certain differences were readily apparent when the clinical pictures of poliomyelitis in the adult and in the child were compared. Although almost none of the features of the disease present in the older patients were absent in younger ones, there was marked quantitative variation in some respects in the two age groups. Thus, certain types of prodromal manifestations were much more prevalent in the adult than in the child. Chills, urinary retention, muscle pains, skin eruptions, ocular-muscle palsies and medullary involvement were of much greater frequency in the adult group. In these hospitalized children, males tended to be affected more often than females; in older patients, the sex distribution was about equal or there was a slight preponderance of females even when the increased susceptibility due to pregnancy was taken into consideration. Although there was only a small difference in incidence of the paralytic disease in the two age groups, involvement was usually more extensive in the adult than in the child. Weakness of the diaphragm and of back and chest muscles was more common in older patients. Whereas involvement of one leg was the commonest type of paralysis in children, adults suffered quadriplegia most often. The rising degree of severity of poliomyelitis with increasing age was reflected in the case-fatality rate, which was 9 times greater in adults than in children. The important differences between poliomyelitis in adults and in children that were noted in this investigation are presented in Table 8.

These studies point out the growing importance of poliomyelitis in the field of internal medicine because of the increasing number of adults who are contracting this illness. In the past it has been mainly the pediatrician, orthopedist or neurologist who has been interested in this disease, and the internist has tended to neglect it if for no other reason than that it rarely came to his attention.

Table 8. *Clinical Differences in Poliomyelitis in Adults and Children: 428 Hospitalized Patients, 1949.*

Clinical Features	Children	Adults
Sex incidence	More males	More females
Severity of disease	Relatively mild	Severe
Commonest prodrome	Upper-respiratory infection or none	"Grippe" or none
Chills	Uncommon	Common
Gastrointestinal disturbances	Uncommon	Common
Bladder paralysis	Uncommon	Common
Lymphadenopathy	Common	Uncommon
Skin eruptions	Uncommon	Common
Commonest type of bulbar disease	N IX, X, VII	N VII, IX, X, III, IV, VI and medulla
Commonest paralysis of extremities	One leg or one arm	Both arms and both legs or both arms
Paralysis of respiratory muscles	About 10 per cent	About 40 per cent
Paralysis of muscles of abdomen and back	About 20 per cent	About 35 per cent
Cyanosis	Rare	Common

The acute phase of all forms of poliomyelitis, — particularly if the respiratory mechanism is involved or the bladder is paralyzed or secondary infections supervene, — primarily constitutes a problem in general medical care. Recent studies that have revealed serious involvement of cardiovascular structures and function emphasize the purely medical aspects of the problem.[8] Because poliomyelitis in the adult tends to be more severe than in the child, the management of a case constitutes a much more serious problem for the internist than for the pediatrician, as most of his patients have relatively mild infections and the case-fatality rate in children is relatively low.

Conclusions

The prodromal manifestations and clinical course of poliomyelitis in adults and children are quantitatively different.

The difference in incidence of various types of paralysis in adults and children is relatively small.

When paralysis occurs, it tends to be more widespread and severe in the adult than in the child; bulbar involvement is more extensive and medullary disease more common in the older age group.

Paralyses that endanger life are more frequent in adults than in children.

The death rate is considerably higher in adults than in children.

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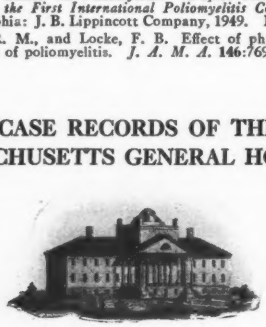
CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL



Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38081

PRESENTATION OF CASE

A sixty-seven-year-old woman was admitted to the hospital because of dyspnea, orthopnea and ankle edema.

For approximately one year prior to entry the patient had complained of poor circulation in the lower extremities. Six months prior to admission she noted exertional dyspnea that was relieved by rest and was not associated with any chest pain. The dyspnea gradually became more severe, and she developed orthopnea, slight ankle edema and a nonproductive cough. Four months before admission, when the symptoms became worse, she was admitted to another hospital, where she remained for five weeks. She responded well to treatment with Crystodigin, ammonium chloride and Mercuhydrin, but after one week she developed digitalis intoxication and this drug had to be discontinued. Ammonium chloride and mercurial diuretics were continued during the remainder of the hospital stay and after discharge, but in spite of these she continued to have mild ankle edema, dyspnea, orthopnea, rales at both lung bases, abdominal distention and hepatomegaly. Two and a half weeks prior to entry these symptoms became much worse, and digitalis (whole leaf, 0.1 gm. every three days) was added to the regimen, but after two weeks this had to be discontinued because of signs of digitalis intoxication. She was admitted to another hospital, where she was found to have bigeminal rhythm, moderate ankle edema, rales at the left base, a right pleural effusion and a low-grade fever; the nonprotein nitrogen was 66 mg. per 100 cc. and the serum sodium and chloride were normal. She received penicillin intramuscularly, ammonium chloride and mercurial diuretics. She became drowsy and slightly disoriented and had anorexia, nausea and vomiting. She had not received digitalis for five days prior to admission.

Her general health and strength had always been good. For five years she had had paresthesias in the arms and legs. Examination in the Out Patient Department five and three years prior to entry had disclosed no evidence of organic disease, and the laboratory studies were normal; the blood pressure was 142 systolic, 78 diastolic.

Physical examination revealed a drowsy, slightly confused, dehydrated, dyspneic and orthopneic woman, who was slightly cyanotic. The neck veins were distended. There were decreased respiratory excursions of the left chest posteriorly, dullness to percussion and absent breath sounds at the right base and moist rales at the left base. The heart was enlarged to the anterior axillary line; sounds were of poor quality, with bigeminy and coupling pulsus alternans. There was a Grade II apical systolic murmur, with a Grade III harsh diastolic murmur heard along the left sternal border. The pulmonic second sound was louder than the aortic. Examination of the abdomen revealed shifting dullness and a fluid wave. A slightly tender liver was palpable 2 fingerbreadths below the costal margin. There was ++ pitting edema of the legs and ankles. Dorsalis-pedis pulses were not palpable.

The temperature was 98.6°F., the pulse irregular, varying between 60 and 80, and the respirations 28. The blood pressure was 110 systolic, 70 diastolic.

The urine had a specific gravity of 1.011 and gave a +++ reaction for albumin; the sediment contained an occasional white cell and cellular cast. Examination of the blood showed a hemoglobin of 12 gm. and a white-cell count of 10,300, with 83 per cent neutrophils. The nonprotein nitrogen was 106 mg. per 100 cc.; the sodium was 123.1 milliequiv., the chloride 83 milliequiv., the

potassium 5.6 milliequiv. and the carbon dioxide 17.9 milliequiv. per liter. An electrocardiogram showed a nodal rhythm at a rate of 50 with multiple premature ventricular beats, a QRS interval of 0.16 second and normal voltage. There were wide slurred R waves in Leads 1, AVL, V_6 and V_7 and wide, slurred S waves in Leads 2, 3, AVF, V_1,V_2, V_3, V_4, V_5 and V_8. A chest roentgenogram showed the heart to be considerably enlarged; its size could not be adequately determined because of the presence of fluid in the right pleural cavity. The pulmonary vascular shadows seemed fairly prominent. There were linear scars in the lateral portion of the left chest (Fig. 1). Three hundred

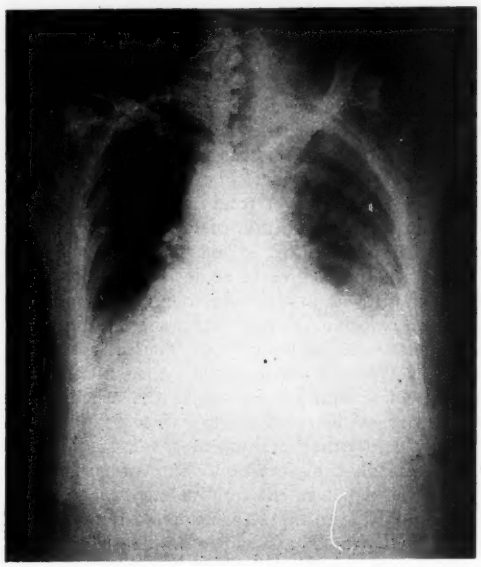


FIGURE 1.

and fifty cc. of cloudy-amber rapidly clotting fluid was removed from the right pleural cavity; this had a specific gravity of 1.010, contained 72,000 red cells per cu. mm. and showed no growth on culture.

After thoracentesis the patient was placed in an oxygen tent and was much more comfortable. Thirteen hours after admission, after taking some medication, she suddenly gasped for breath, became very cyanotic and died within a few minutes.

DIFFERENTIAL DIAGNOSIS

DR. ERNEST CRAIGE*: May I see the x-ray films first, Dr. McCort?

DR. JAMES J. MCCORT: A moderate amount of fluid is present in the left pleural cavity and there is a greater amount in the right; this fluid partially obscures the lower lung fields, but there is no evidence of underlying consolidation. A slight reduction in size of the left lower lobe may be due to compression by fluid. In the lateral margin of the left lung there are a few strands of increased density that may represent scars or focal areas of atelectasis. Gross enlargement of the heart is present, but I cannot make out isolated chamber enlargement because of the overlying fluid; that is, the heart is without a characteristic configuration. A slightly sclerotic and tortuous aorta is seen (Fig. 1).

DR. CRAIGE: This elderly woman was getting along rather well until six months before she came here, when she had the onset of symptoms that may be grouped together under the heading of left-ventricular failure. She noted the onset of dyspnea on exertion, orthopnea and a nonproductive cough, followed soon by signs of right-ventricular failure, enlargement of the liver, ascites and edema. Subsequently, she was found to have a very large heart, with pathologic murmurs and a grossly abnormal electrocardiogram. We can assume, then, that the major source of the difficulty lay in the heart. There are three chief questions I should like to try to answer here. First: What was the etiology of the heart disease? Secondly: Was there important disease in other organs of the body that contributed to the relentlessly downhill course? Thirdly: Why was she so unusually resistant to the measures that are ordinarily helpful in congestive failure?

The illness began without any pain, but that in itself does not eliminate the possibility that the difficulty was primarily on the basis of coronary disease. She developed some dyspnea on exertion that was relieved by rest. In elderly patients the symptom of dyspnea often overshadows or is confused with the compression in the chest that may represent angina pectoris. Perhaps the event that led to the hospitalization four months before admission here was a myocardial infarction resulting in pulmonary congestion. I am not told whether she had any murmurs during that admission or what the electrocardiogram or x-ray films showed. It would have been helpful, perhaps, to have an electrocardiogram, particularly if there was myocardial infarction. The disintegrating record, which is given at the end of the protocol, does not give me much help as regards the etiology. The electrocardiogram shows rather bizarre ventricular complexes. The rhythm is nodal, with ectopic ventricular contraction.

She became toxic to digitalis and the drug had to be stopped after a few days. After five weeks in the hospital she was discharged, still in congestive failure, although perhaps somewhat better than on admission. Some six weeks later, because of an abrupt deterioration in her condition, she

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re-entered the other hospital, where she again became toxic to small amounts of digitalis and developed a bigeminal rhythm. She also showed a right-pleural effusion and a low-grade fever. The mild elevation of the nonprotein nitrogen may have been due to congestive failure with poor renal blood flow. The fever is not accounted for purely on the basis of congestive failure and brings up the possibility of complicating infection or infarction, possibly in the lung. The nausea and vomiting can be explained on the basis of digitalis intoxication with some congestion of the abdominal viscera; probably the increasing azotemia also contributed to the nausea.

The past history is of interest in that the normal physical examinations repeatedly recorded in the Out Patient Department help me to rule out old rheumatic, syphilitic and hypertensive heart disease. The absent pulses in the feet in a woman of this age are probably due to arteriosclerosis and not to coarctation of the aorta.

On admission here she appeared severely ill and dehydrated, with signs of fluid in the chest and the abdomen, and had an increased venous pressure in the neck. The heart was very large. The description of the murmur is confusing. She had a Grade III harsh diastolic murmur along the left lower sternal border and also an apical Grade II systolic murmur. These murmurs had not been described previously, either in the Out Patient Department or in the other hospital. The diastolic murmur, then, was apparently of recent origin. I am not told much about its timing — whether it was mid-diastolic or early diastolic, or whether it was decrescendo or crescendo. Its location along the left sternal border suggests that it may have originated at the aortic valve, although occasionally a mitral diastolic murmur may be heard medial to the apex as well as at the apex. Sometimes we hear diastolic murmurs from the tricuspid valve in this location. If the murmur actually appeared very recently, one might expect to find on the aortic valve a destructive process such as a bacterial endocarditis. There was, however, no supporting evidence for this diagnosis, in the form of either peripheral emboli or aortic regurgitation. I am, therefore, going to rule out bacterial endocarditis on the aortic valve as being responsible for this murmur. As a matter of fact, I am a little loath to accept the description of the murmur at face value, anyway.

Dr. Max Rukes: A murmur was heard throughout diastole, without crescendo or decrescendo, along the left sternal border; a systolic murmur was heard throughout the systolic phase, without crescendo or decrescendo, at the apex.

Dr. Craige: Thus, a long diastolic murmur was heard consistently along the left sternal border throughout the time that this patient was in the hospital, but it was not present on previous occasions. This diastolic murmur is hard to explain on the basis of suddenly appearing aortic or mitral disease. I would prefer to say it originated from the tricuspid valve in this acutely dilated heart. A systolic murmur or a diastolic gallop in this location may develop with a right ventricle dilated, from a variety of causes, either in the course of chronic cor pulmonale or more abruptly with an acute cor pulmonale.

The urine showed a low specific gravity and occasional casts. Congestive failure alone may account for the findings, although the low specific gravity would bring up the additional possibility of primary kidney disease, as does the rather high figure to which the nonprotein nitrogen eventually rose. The blood chemical determinations give some valuable information about the patient's poor response to therapy. She was dehydrated, yet the extracellular-fluid volume was increased, accumulating in the dependent portions of the body and causing ascites and edema. Sodium and chloride were present in a much reduced concentration, the chloride being the more seriously depleted. The patient was acidotic, as is indicated by the reduced carbon dioxide. The problem was to have her lose water and yet retain sodium and chloride. Patients in this condition of ionic imbalance, however, are unable to respond to mercurial diuretics. With this degree of acidosis and poor kidney function, it was inadvisable to give her more ammonium chloride. Furthermore, she had repeatedly been shown to be toxic to very small amounts of digitalis without receiving any benefit from this drug. On several admissions to the other hospital there was evidence of digitalis intoxication, — bigeminy and other arrhythmias, — and finally, in this hospital, complete depression of auricular activity was shown in the terminal electrocardiogram.

I should like to think that she had two main conditions. I would attribute the heart disease to coronary arteriosclerosis, and I suspect that the patient had a myocardial infarction four months before her admission here. I would explain the appearance of bloody pleural effusion, the stepwise downhill course and the failure to respond to treatment on the basis of pulmonary emboli.

Clinical Diagnoses

Arteriosclerotic heart disease.
Digitalis intoxication.
?Low sodium syndrome.

Dr. Craige's Diagnoses

Coronary heart disease with myocardial infarction, old.
Pulmonary emboli.

Anatomical Diagnoses

Primary amyloidosis of heart with cardiac failure.
Amyloidosis of spleen, lung and blood vessels.
Bronchopneumonia.
Pleuritis, acute, with effusion.

Pathological Discussion

Dr. Benjamin Castleman: We did not expect Dr. Craige to make the correct diagnosis, as this is the first case like it that we have ever had. We found the heart to be enlarged, weighing almost 400 gm., dilated and peculiarly solid, for the muscle throughout the left ventricle was thick, — not flabby, — and seemed to hold its shape. Mural thrombi were present in both auricular appendages. Outside of that there was nothing wrong with the heart that we could make out in the gross. Although we believed there was something peculiar about it, we did not know just what it was. The lungs showed evidence of bronchopneumonia. There was slight acute pleurisy on the right and some fluid in both pleural cavities.

Figure 2. *Photomicrograph of Myocardium. Note diffuse amyloidosis in lower portion and amyloid rings in upper portion.*

The clue to the diagnosis at the time of autopsy came from the spleen, which, although not enlarged, appeared somewhat waxy, suggesting the possibility of amyloid. This possibility was then transferred to the heart, and that is what it turned out to be. This slide of the heart muscle demonstrates very little normal heart muscle, the latter being replaced by amyloid (Fig. 2). Even in this low-power view, the amyloid rings around the muscle fibers, imprisoning the individual muscle fibers, are well demonstrated. Apparently the amyloid was deposited around the muscle fibers, enclosing them so completely that the fibers degenerated. It is true that we have seen amyloid in hearts before, but this is the first case in which it has been of sufficient magnitude to produce heart failure. There was no source for any secondary amyloidosis, and the only other organs that were involved were the spleen and parts of the lungs, which is often seen in the so-called primary amyloidosis, as well as the vessel walls in many organs of the body. The kidneys were normal and showed no suggestion of amyloid except for a little in a few of the arteries, but the tufts and tubules did not show any amyloid. There was no evidence of myeloma, which is occasionally seen with amyloid.

Dr. Howard B. Sprague: How about the coronary arteries?

Dr. Castleman: The coronary-artery walls showed arteriosclerosis. The endocardium was very thick and contained large deposits of amyloid but none that we could make out in the gross as little nodules, which are sometimes seen in the endocardium of the chambers as well as of the valves.

Dr. James H. Currens: The valves were normal?

Dr. Castleman: Yes; I cannot account for the murmur.

CASE 38082

Presentation of Case

First admission. A fifty-three-year-old woman was admitted to the hospital because of right-chest pain and increasing dyspnea.

For the ten years prior to entry she had had a chronic cough that had gradually become more severe. Five years before admission she first noted shortness of breath; this too was progressive. X-ray films of the chest taken two years before entry were interpreted as "consistent with advanced tuberculosis," but sputum examinations and a tuberculin test were negative. Potassium iodide and "short-wave therapy" had no effect on the progress of the symptoms; the cough became especially severe in the mornings and was frequently productive of about one-half cupful of white sputum, which on rare occasions was blood streaked. One year prior to admission she had a spontaneous right pneumothorax from which she gradually recovered without hospitalization or specific therapy, but following this there was marked shortness of breath, 2-pillow orthopnea, tachycardia and moderate weight loss.

There was no history of exposure to metallic or other toxins. Whooping cough occurred once in childhood and again (a severe attack) about ten

years before entry. There was no history of chills, fever, night sweats, anorexia, nausea, vomiting or change in bowel habits. Mild nocturia, dyspareunia and leukorrhea had been present for years.

Physical examination revealed a thin woman with dyspnea and orthopnea. The fingers were cyanosed. The trachea was deviated to the right. The right chest was hyperresonant. There were diminished breath sounds and vocal fremitus over the right upper lobe and absent breath sounds and tactile fremitus over the right lower lobe posteriorly. The left diaphragm was higher than the right, which did not move with respiration. Many inspiratory and expiratory squeaks were heard on the left. The heart was enlarged on palpation. The pulmonic second sound was greater than the aortic. The liver and spleen were palpated 2 cm. below the costal margin. Pelvic examination revealed some leukorrhea, and manipulation of the cervix caused severe pain.

The temperature was 101°F., the pulse 128 and the respirations 30. The blood pressure was 120 systolic, 70 diastolic.

The urine gave a ++ albumin reaction. Examination of the blood revealed a hemoglobin of 15.1 gm. and a white-cell count of 10,600, with 80 per cent neutrophils. The total protein was 6.20 gm., the albumin 3.7, the globulin 2.5 gm. and the nonprotein nitrogen 25 mg. per 100 cc. A cephalin-flocculation test was +++ in 48 hours. Several stools were guaiac negative.

An x-ray film of the chest revealed a pneumothorax on the right side (Fig. 1). The pleura was separated for a distance of 1 cm. at the apex and at the base for a distance of 4 cm. There was a coarse, stringy increase in density throughout both lung fields, with some thickening of the visceral pleura. There were small radiolucent areas, which had the appearance of blebs. The heart was small. X-ray films of the hands showed radiolucent areas in the head of the proximal phalanx of the left index finger and in the base of the proximal phalanx of the right index finger. There were small oval radiolucent areas throughout the proximal phalanges of the other fingers in the right clavicle. The articular surfaces were smooth without erosion.

Following preliminary penicillin therapy a trochar thoracotomy was performed on the right side and the air in the pleural cavity was aspirated. She was discharged somewhat improved on the sixteenth day.

Second admission (one year later). In the interval the patient had continued to be dyspneic and to have a fairly severe cough. Three days prior to admission the cough increased in severity, and she developed a shaking chill and a high fever accompanied by extreme dyspnea. The cough was productive of copious greenish mucopurulent sputum, which was not blood stained. There was no chest pain.

Physical examination revealed a very anxious, dyspneic and cyanotic woman in acute respiratory distress. Chest expansion was limited bilaterally. There was decreased resonance in the right paraspinal region and in the lower right axilla. There were bronchial breath sounds and increased tactile and vocal fremitus over the right middle and lower and left lower lobes. No rales were heard, but extensive squeaks and groans were present. The apex of the heart could not be felt. Abdominal examination was negative.

The temperature was 105°F., the pulse 144 and the respirations 32. The blood pressure was 95 systolic, 75 diastolic.

Urinalysis showed a + albumin reaction. The hemoglobin was 14.5 gm. and the white-cell count 24,000, with 90 per cent neutrophils. The serum sodium was 126.4 milliequiv., the chloride 88 milliequiv. and the carbon dioxide 35 milliequiv. per liter. Smears of the sputum showed no bacteria but abundant polymorphonuclear leukocytes. Sputum cultures grew abundant oval-bodied yeast and a moderate growth of *Hemophilus influenzae*. X-ray films of the chest revealed obliteration of the old pneumothorax, with only a small collection of air remaining (Fig. 2). An accumulation of fluid was noted in the pleural space of the upper half of the right lung, and there was a suggestion of fluid along the right side of the superior mediastinum. There was extensive fibrosis and bleb formation throughout both lung fields.

FIGURE 1.

There was no response to therapy with penicillin, streptomycin and Chloromycetin. She continued to have a spiking temperature of 100 to 103°F. daily. She died quietly on the eleventh day, after a number of hours during which her respirations were 5 to 6 per minute.

Differential Diagnosis

Dr. Helen S. Pittman*: This woman had chronic pulmonary disease with chronic disease in many other parts of the body and then was admitted with an acute, rapidly fatal terminal episode.

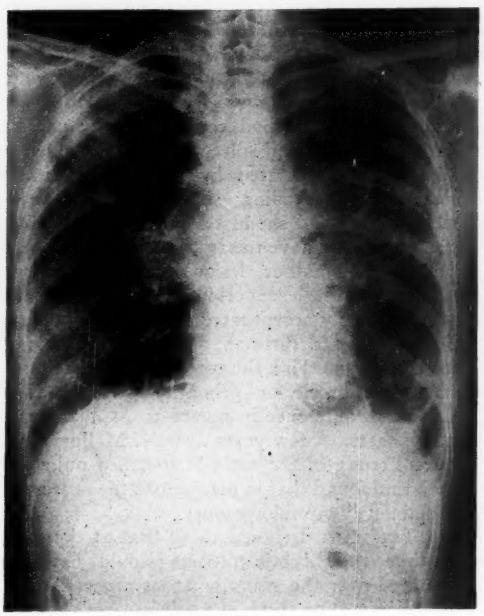

Figure 2.

"The trachea was deviated to the right." I question that, in view of the x-ray findings. May I see the x-ray films?

Dr. Stanley M. Wyman: We have films taken at an outside radiology office about three and a half and two and a half years prior to admission and films taken here at both admissions.

Changes are pronounced on the earliest films; they consist of extensive perihilar fibrosis and infiltration, with probable enlargement of the hilar lymph nodes and extensive infiltration into both lung fields. This process progresses during the course of the examination, and large blebs are formed. The enlargement of nodes is obscured in the later films by the degree of fibrosis in the hilar region, and one cannot be certain how much lymphadenopathy persists. Films taken in the hospital show the large basal pneumothorax and a small peripheral pneumothorax on the right. The trachea, as Dr. Pittman predicted, does not deviate very significantly. The last film shows a further progression of the described process, with now huge clear spaces that appear to be in the lung itself rather than in the pleural space, in all probability. I would interpret these as being huge bullae rather than pneumothorax, although I cannot prove my point. Elsewhere there is increased prominence of bullae. Changes in the bones of the hands are as described and consist of rarefactions in several phalanges and possibly in the right carpal scaphoid.

Dr. Pittman: I should like to discard most of the possibilities that may be discussed at length in a differential diagnosis; among those are infections — such as tuberculosis, fungus disease, brucellosis and leprosy. I do not think there is any reason to consider neoplasm. The history states that she had not been exposed to toxic agents; I see in the audience physicians who are interested in toxicology; maybe something has turned up subsequently that did not appear in the history. I think what I am dealing with is a diffuse granulomatous process. It seems to me that it should have been due to sarcoid; it could have been due to beryllium.

What do I find in the record that is really important? First of all, this woman had long-standing disease that was insidious in its onset and began with cough; then, after a matter of some years, she had shortness of breath. She apparently had x-ray changes when she was first examined, which was about eight years after the onset of the vague symptoms. This was called "consistent with advanced tuberculosis," which does not mean anything except that something was going on in the chest. I was going to ask about hilar lymph nodes, but I do not need to ask, now that Dr. Wyman has given us the description. She had a negative tuberculin test, which is important contributory evidence toward a diagnosis of sarcoidosis. The test may become positive later on, — a good many patients with sarcoid disease do show tuberculosis eventually, — but the negative tuberculin test at the onset confirms my impression of sarcoid. One year prior to admission she had a right pneumothorax. Persons with granulomatous disease of any etiology may have a pneumothorax caused by rupture of an emphysematous bleb.

I should like to ask Dr. Ingersoll — what was this in the pelvis? I have been able to find reports of granulomatous disease that involved the testes, epididymis and prostate on rare occasions, but I have been unable to find any reference to involvement of the female pelvis.

Dr. Francis M. Ingersoll: I do not know the case, and from the description given in this record I do not think I can make any comment.

*Associate physician, Massachusetts General Hospital.

DR. PITTMAN: I shall ignore it.

What else fits in with the diagnosis of sarcoidosis? This patient probably had a certain degree of cor pulmonale. The pulmonic second sound was greater than the aortic. In many patients with fibrosis due to a granulomatous process there is pulmonary hypertension from encroachment on the pulmonary vascular bed, and in some of them a cor pulmonale develops. The patient had an enlarged liver and spleen and evidence of disturbed liver function, as shown by a cephalin-flocculation test of +++ in 48 hours. In Riley's series[1] of 52 cases of sarcoidosis from the Bellevue Hospital almost half had involvement of the liver and spleen — next most common to enlarged mediastinal nodes. The final point by which I am influenced is that she had bone changes consistent with sarcoidosis; these changes, I believe, occur in only 10 to 15 per cent of cases. We seldom see them in the Pulmonary Clinic. Maybe beryllium produces lesions like that; again I am not sure. When the patient first came in, the Service apparently relieved the chest pain by a tap by which the pressure of the pneumothorax was reduced, and she was discharged without much real change. At home she grew slightly worse, as one does with a chronic disease of this sort. Then something happened; three days before she was admitted for the second time she had a shaking chill, a high fever and extreme dyspnea. I shall have to assume that this was intercurrent infection. I should have mentioned the productive cough and the systemic changes that she had in the past and that accompany the bronchiectasis that may develop in a process such as I believe this woman had. On admission she had a high temperature and a leukocytosis of 24,000 with 90 per cent neutrophils. Did she have any consolidation that you can see, Dr. Wyman?

DR. WYMAN: I cannot recognize any frank consolidation.

DR. PITTMAN: She had further trouble in the lungs. The sputum culture grew yeast and *H. influenzae*. Whether they were the etiologic organisms for the acute episode or whether they just happened to be there I do not know.

Now I come to the observations that relate to a point of recent interest — the disturbance of the sodium, chloride and carbon dioxide. This woman had been extremely dyspneic for years; she had fibrosis, much dead space in the lungs, and emphysema, and she had been unable to blow off carbon dioxide. I should like to know whether or not, in this last admission, when she was treated with penicillin, streptomycin and Chloromycetin, she also had oxygen.

DR. DONALD S. KING: She had lots of it.

DR. PITTMAN: Certainly it is true that many of these patients with a high carbon-dioxide level cannot make the grade when they are given oxygen and are thrown into a dangerous or fatal episode; I think it may be very important that this woman, who came in with respirations of 32 and a carbon dioxide of 35 milliequiv., was given oxygen before she died with respirations of 5 to 6 a minute.

I think it is now time to take up the other side of the case. This woman did not have anemia, which is a common finding in sarcoidosis. She did not have elevation of serum protein — particularly of the globulin fraction, which is elevated in half to three quarters of these patients. She had no skin lesions. No ocular lesions have been mentioned, so I assume she had none.

She did have what seems to me more important — a chronic long-standing disease with a protracted course in which she had cough, insidiously developing dyspnea and sputum. At the onset she had a negative tuberculin test; lesions were demonstrated in the x-ray films, which changed over a period of time; she had cor pulmonale; she had disease of the liver and spleen; she had involvement of the kidney, indicated by the albumin in the urine; she had bleeding; she had a spontaneous pneumothorax; and she lost a great deal of weight. Therefore, I shall have to say that this woman had a diffuse granulomatous lesion that I think was sarcoidosis, with a superimposed acute terminal episode probably accentuated by the use of oxygen.

DR. KING: Dr. Pittman, suppose your diagnosis is correct; do you think the autopsy showed primarily pulmonary fibrosis or primarily granuloma? It makes some difference in regard to ACTH therapy in these cases. A few years ago Dr. Mallory[2] made a careful study of the cases of so-called pulmonary fibrosis and found that in many cases the process was predominantly granulomatous.

DR. PITTMAN: I should think that at the end of this time the fibrotic process would have predominated over the granulomatous process.

DR. KING: You think she still had both?

DR. PITTMAN: I should think it was probably preponderantly fibrosis.

DR. KING: Assuming that there is an acute infection on top of the chronic one, what type of acute process do you expect was found at post-mortem examination in this case?

DR. PITTMAN: That is a good question. I spent about an hour on that, last evening, and I have not decided what she had there. I assume she had a certain number of alveoli filled with exudate of an acute inflammatory nature.

DR. F. DENNETTE ADAMS: Do chills and a sudden onset of fever almost force one to conclude it was a pneumococcus or a Friedländer's infection? It seems to me that they are the organisms that cause a chill at the onset when they invade the lungs. She probably had exudate of a pneumonic process, as Dr. Pittman predicted, based on one of these organisms.

DR. HARRIET HARDY: It is of interest that we have never seen any bone lesions in the x-ray films

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in the series of cases we like to call "chronic beryllium poisoning."

Dr. King: Do you ever see this type of x-ray picture with so much around the hilum in patients with beryllium poisoning?

Dr. Hardy. Yes; we have seen it.

Dr. King: It does not have to be a scattered process?

Dr. Hardy: No; if they live long enough, they may show this type of x-ray picture.

Dr. King: Then does the post-mortem examination show fibrosis or just granuloma?

Dr. Hardy: A great degree of fibrosis.

Clinical Diagnoses

Pulmonary fibrosis and emphysema.
?Sarcoidosis.
Bronchopneumonia.
Pleuritis.

Dr. Pittman's Diagnoses

Generalized sarcoidosis.
Pulmonary infection.

Anatomical Diagnoses

Generalized sarcoidosis with marked pulmonary involvement.
Pulmonary fibrosis with emphysema.
Pulmonary abscesses.
Pleuritis, fibrous, severe.

Pathological Discussion

Dr. Benjamin Castleman: At autopsy, when the chest plate was removed, we found that both pleural cavities were almost completely obliterated by dense fibrous bands, in between which were large loculated areas filled with fluid. Many of these cavities were in between lobes and between the chest wall and the lung itself. When sectioned, both lungs were very mushy and quite airless, and in between these areas were large abscess cavities, — some measuring as much as 8 cm. in diameter, — filled with necrotic material. It seemed as if the lung had become necrotic and the necrotic material had remained there. In between these areas of abscess formation and emphysema, which was very marked, were large foci of fibrosis. The hilar nodes were moderately enlarged and somewhat fibrotic as well. The heart was slightly enlarged, all the enlargement being due to hypertrophy of the right-ventricular wall, which measured 7 mm. — chronic cor pulmonale. The liver was not enlarged — at least it was not heavy. The spleen was enlarged; it weighed over 300 gm. At that size it ordinarily would not be felt, but I suppose that with the long chest both the liver and spleen were pushed down to a point where they both were felt. In the pelvis we found two fibroids.

Dr. Pittman: Anything in the kidneys?

Dr. Castleman: No; they looked normal.

Microscopical examination of this case proved that there was sarcoidosis, as Dr. Pittman predicted. Before showing you the slides of this case I should like to project slides of other cases demonstrating the progression of changes. This first one is from a lymph node with the usual appearance of active sarcoidosis — tubercle-like nodules with Langhans giant cells and without necrosis. The next slide is one in which the process has begun to fibrose, showing the connective-tissue response. The next slide is a further stage, with more scarring. The outcome of these granulomas is certainly not too clear, because there has not been enough good autopsy material to really study them. Some years ago Dr. David Freiman,[3] of our laboratory, tried to follow a number of these cases; he showed that in some cases scarring did occur whereas in other cases there was no change in the sarcoid lesions as long as the patient lived. In the case under discussion there is the organization of these granulomas with extensive fibrosis, which produced a compensatory emphysema, bleb formation and, as occurred at the first admission, a rupture with pneumothorax. The abscesses observed grossly were loaded with yeast organisms and almost certainly had a lot to do with the continuation of the infection within the lung. In sarcoidosis you often see inclusion bodies within the giant cells in the form of a star, called an asteroid body. This case did not have asteroid bodies but did have what have been called Schaumann's bodies in the center of a granuloma. These ringed bodies, which contain iron and sometimes calcium, have been seen in about 10 per cent of our cases of sarcoidosis. They are much more common in the giant cells associated with beryllium granulomatosis. Granulomas were found in the liver, spleen, skin and a few other organs, so this was a systemic case of sarcoidosis with predominant findings in the lung. It is interesting that some of the lesions in the spleen and liver were still quite active and showed very little fibrosis.

Dr. Robert L. Berg: From the autopsy findings alone could you say that it was not beryllium?

Dr. Castleman: No; I do not think you could. I think the finding of the lesions in the hands is perhaps more in favor of sarcoidosis. We have had, as Dr. King mentioned, 6 cases, reported by Dr. Mallory[2] a few years ago, of fibrosis of the lungs with this picture, which I think is perhaps a form of sarcoidosis. It is interesting that in some of these cases there were no lesions in any organ except the lung. I believe we have good evidence to call this case one of sarcoidosis; we are, however, having some of the material analyzed for beryllium.

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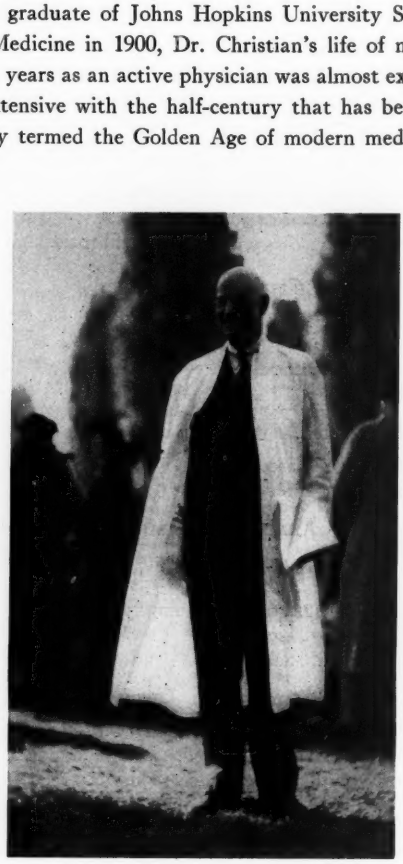
POSTSCRIPTUM

THE first article in this issue of the *Journal*, "Ebbs and Flows in Medical Interest," was submitted by Dr. Christian only a few weeks before his death on August 24, 1951, and must perforce be published posthumously. This postscriptive quality gives it the added dignity of being presumably his last written statement of professional importance, constituting a review of the events in medicine that he had witnessed and in which he had participated so conspicuously.

For Dr. Christian was one of that group of robust engineers of medical progress who, after Osler, bridged the gap between the old and the new in medicine — between the period of observation and description, with a major reliance on pathology, and that of experimentation and the prevention of disease.

A graduate of Johns Hopkins University School of Medicine in 1900, Dr. Christian's life of nearly fifty years as an active physician was almost exactly coextensive with the half-century that has been so aptly termed the Golden Age of modern medicine.



Caring to be not too often the first by whom the new was tried, he was yet never the last to lay the old aside. Combining the care of the patient with the scientific spirit of research, he remained throughout his life precise in observation and in the recording of his observations and earnest in the training and guidance of young men.

INTERNSHIP MATCHING PLAN

DURING the current year a plan has been put into operation, — for the first time on a national basis, — whereby it is hoped that the knotty problem of hospital internship may be resolved. This plan is expected to provide graduating medical students with the most desirable internships for

which they can qualify and at the same time to provide the hospitals "approved" for such internships with the best selection of young men from among these graduates who desire the type of training afforded by these hospitals. The plan is admittedly an experiment designed to avoid the many unpleasant experiences that have resulted in the past few years from the unbridled competition attending the selection of interns in many parts of the country.

The general plan finally adopted by the National Interassociation Committee on Internships, after some misunderstandings were ironed out, was essentially a modification of the "Boston pool" plan of matching, which has been in successful operation among Boston's major teaching hospitals for a number of years. This plan offers both hospitals and prospective interns ample opportunity for acquaintance with one another prior to the final acceptance of interns on the one hand and appointments on the other. Under the plan the student is required to submit to a central office a confidential listing of the hospitals in which he is willing to accept an internship, arranged in the order of his preference, and the hospitals, after they have surveyed the students, — through letters of recommendation, interviews or examinations, — likewise submit to this office a similar confidential list of candidates who have indicated an interest in that hospital, also in the order of their acceptability to the hospital. By a prearranged plan and under prescribed rules the preferences are matched against each other, and as far as possible the hospital given the highest rating by the student is matched to the hospital that has given the student the highest rating.

This plan is sponsored by the following groups: American Hospital Association, Association of American Medical Colleges, Catholic Hospital Association and Council on Medical Education and Hospitals of the American Medical Association, with liaison members from the Air Force, Army, Navy, Public Health Service and Veterans Administration. The national students' organizations concerned with internships have been consulted. By December 1, 1951, all but 16 of the hospitals approved for internship had agreed in writing to participate in this co-operative plan. Over 5600 senior medical students had likewise agreed to abide by the rules of the committee. The plan is designed to preserve free choice by both hospitals and students, as well as their bargaining rights, and not to interfere with but to give effect to the preferences of both. The national organization handles only the administrative details of the operations necessary to carry out this matching system in a totally unbiased manner.

Students participating in the plan have agreed, over their signatures, to make no commitments or contracts with hospitals prior to the notification of the results of the matching plan. Participating hospitals, in turn, have agreed, over the signatures of their authorized agents, to make or require no commitment or contract prior to the notification of the results of the plan. Of course, after the matching has been completed and the results announced, any student who fails to obtain an internship that matches one of his choices may then enter into direct negotiations for any of the positions remaining vacant. It is anticipated that there will be a considerable number of such positions.

Even before the plan has progressed beyond its initial phases, reports are being circulated of hospitals that are requiring students to promise top preference if they are to be considered. In some instances the one who signed the contract for the hospital has made or asked for no commitments, but other interviewers have made direct proposals or threats or attempted to obtain definite commitments. Of course, such proposals cannot be considered binding, since each of the parties could make any number of verbal promises and yet record in his official listing only his actual preferences. The choices remain confidential until the time of the actual matching.

It seems almost unthinkable that in this day any physician, — particularly one in a responsible position in medicine, — should be counted among those who think lightly of agreements that they have made apparently in good faith and of their own free will. Nevertheless, some outstanding physicians and teachers in a number of the country's leading medical schools seem to have done exactly that. This failure to abide by a signed agreement in what

is obviously an honest experiment undertaken to solve a difficult problem must be taken as an admission of personal insincerity, unwillingness to undertake the task of properly presenting the facilities of their institution to the best available candidates, or lack of faith in the workings of the experiment in which they agreed to participate. There is no more certain way to ensure the failure of any venture than the failure of a significant segment of the participants to co-operate.

It is unfortunate, of course, that the medical students, who may still be considered in a formative stage with respect to their ethics and attitudes, should be confronted with such unwholesome practices by their superiors and future chiefs. By requiring students to make prior commitments the hospital chiefs have asked them to repudiate their signed agreements. However, it is to be hoped that these current graduates will set an example by holding to their own free choices against the direct or implied threats of their elders.

It is highly important that this new venture succeed, and it is to be hoped that those students and hospitals who co-operated in the spirit and letter of the agreement will be satisfied with the results. Presumably the transgressors are those who have had little or no experience with such plans in the past, and the successful operation of this plan should convince them that such transgressions are to no one's interest.

MEETING OF THE COUNCIL

THE Council of the Massachusetts Medical Society held its stated midwinter meeting on February 6 in John Ware Hall, Boston Medical Library, with President W. Richard Ohler in the chair and Dr. Thomas H. Lanman acting as Secretary in the absence of Dr. Gallupe. Two hundred and fifty-two councilors were present. The deaths of two councilors since the fall meeting were reported, those of Patrick E. Gear of Hampden and Percy J. Look of Essex North.

President Ohler then announced the resignation of Dr. Ralph R. Stratton from the vitally important Committee on Ethics and Discipline. Dr. Stratton has been a member of this committee for fourteen years and was its chairman for ten of them; his name has become synonymous with personal integrity, discerning judgment and a high sense of moral values. The chairmanship thus made vacant will be filled by Dr. Joseph C. Merriam of Middlesex West, and Dr. Stratton's place on the Committee will be taken by Dr. Allen S. Johnson of Hampden. Dr. Horatio Rogers of Suffolk was nominated as chairman of the State Civil Defense Training Committee.

The actions taken by the Council were about evenly divided between the negative and the positive. It defeated the resolution that Norfolk District Society requested be introduced into the House of Delegates of the American Medical Association urging a revision of the draft law to extend to age fifty-five the liability of physicians to service under it, and it passed Norfolk's proposed resolution to the same body asking that the method of classifying services of a hospital in terms of years, as announced by the American Board of 1949, be reconsidered and modified.

The controversial and difficult matter of the assignment of Blue Shield fees collected on the account of ward patients, especially in teaching hospitals, and the division of fees between surgeons and assistants elicited a spate of discussion. It illustrates the old contention that in many disputes there is no clear-cut issue between right and wrong but only a fine line, sometimes difficult to draw, between the opposing points of view. The question was finally referred back to the Subcommittee on Blue Cross–Blue Shield Problems for further deliberation, as had been recommended by the Executive Committee.

The report of the Committee on Finance, presenting a budget for 1952 of $185,838 in comparison with that of $181,011 for 1951 was accepted, a plea being made in this relation for a better co-ordination of the Society's business.

In reference to the present method of electing delegates to the American Medical Association on nomination by the President, Dr. N. S. Scarcello, of Worcester, introduced a motion calling for a change in the by-laws to provide for the nomination of delegates by the Committee on Nominations or from the floor — the latter being possible under the present by-laws. The motion was referred to

the Committee on By-laws and Council Rules. A letter from the Secretary of the American Medical Association was read that announced the loss of a Massachusetts delegate. Fewer than 6000 of the more than 6000 eligible fellows of the Society having paid their dues to the Association for 1951, the representation is thus automatically reduced from seven to six. This loss of voting power in the national councils can be restored only by the personal action of the defaulting fellows.

"BETTER TO SERVE"

THE advance notice, published elsewhere in this issue of the *Journal*, of a postgraduate course in obstetrics and pediatrics to be given jointly by the Boston Lying-in and Children's hospitals in April is an additional reminder of the growing part that postgraduate instruction is playing in practical medicine.

Similar reminders are to be found in every issue of the *Journal*, for its organizational pages are replete with notices of meetings to be held, at various grades from the local-society level up to the rarefied atmospheres in which the international associations hold their Olympian conferences. A week ago the program of the seventh annual postgraduate lecture course arranged under the joint sponsorship of the Massachusetts Medical Society and the State Department of Public Health was published; in September the second annual Western Massachusetts Postgraduate Medical Conference was announced and came off according to schedule; and in November the tenth New England Postgraduate Assembly, sponsored by the medical societies of the six New England States, took place in Boston.

The annual meetings of the Massachusetts Medical Society itself, held without fail for 170 years, provide a classic example of the need of educated men to exchange their ideas and to benefit thereby. The Survey of Postgraduate Medical Education that is now being conducted under the sponsorship of the Society's Committee on Postgraduate Education represents the Society's newly organized plan "for improving and expanding opportunities for postgraduate medical education in Massachusetts."

In fact, the pages of nearly every medical journal constitute an extension course in postgraduate medical instruction.

The injunction carved over the main gate of Harvard's Yard, "Enter to Grow in Wisdom," could as well be part of the instruction given to each new member of the Massachusetts Medical Society. The inscription that one sees on leaving those academic precincts might be slightly altered for the purposes of the Society to read "*Remain*, better to serve thy country and thy kind!"

HEART FUND

Readers of the *Journal* are reminded of the current campaign for funds of the American Heart Association, which closes on February 29. Never before have dollars been so plentiful; never before have they been so needed.

During the last three years, the wives of 9 men have been brought to the Massachusetts State Lunatic Hospital, at Worcester, in consequence of their husbands going to California.

Boston M. & S. J., *February 25, 1852*

Fourth-year students in approved medical schools are reminded that the *Journal's* prize essay contest closes on March 15, by which date manuscripts must be in the hands of the editor.

For further information the reader is referred to the *Journal* of October 4, 1951, page 547.

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

CALITRI -- Constant Calitri, M.D., of Lawrence, died on January 16. He was in his sixty-fifth year.

Dr. Calitri received his degree from the University of Maryland School of Medicine in 1907. He was a member of the Greater Lawrence Medical Society and a fellow of the American Medical Association.

His widow and three children survive.

FISHMAN — Maurice Fishman, M.D., of Lowell, died on November 30, 1951. He was in his sixty-first year.
Dr. Fishman received his degree from Tufts College Medical School in 1910.
His widow and two children survive.

GEAR — Patrick E. Gear, M.D., of Holyoke, died on January 20. He was in his fifty-ninth year.
Dr. Gear received his degree from Harvard Medical School in 1919. He was a member of the Holyoke Medical Society, the American College of Surgeons, the American Urological Society and the Springfield Academy of Medicine. He was a fellow of the American Medical Association and a former president of the Hampden District Medical Society. At the time of his death he was a councilor of the Massachusetts Medical Society.

MOLOTCHICK — Maxwell B. Molotchick, M.D., of Lynn, died on January 15. He was in his fiftieth year.
Dr. Molotchick received his degree from the Middlesex University School of Medicine in 1928.

O'DAY — George F. O'Day, M.D., of Worcester, died on January 18. He was in his seventy-eighth year.
Dr. O'Day received his degree from Harvard Medical School in 1901. He was a fellow of the American Academy of Physicians.

PRATT — Ezekiel Pratt, M.D., of Brewster, died on January 19. He was in his sixty-sixth year.
Dr. Pratt received his degree from Harvard Medical School in 1912. He was a former president of the Arlington Doctors' Club and a fellow of the American Medical Association.
His widow and four children survive.

WOOD — Nathaniel K. Wood, M.D., of Boston, died on January 3. He was in his seventy-sixth year.
Dr. Wood received his degree from Harvard Medical School in 1901. He was a member of the American Climatological and Clinical Medicine Association and a fellow of the American Medical Association.
Two brothers survive.

WOODMAN — Ernest L. Woodman, M.D., of Marblehead, died on November 7. He was in his fortieth year.
Dr. Woodman received his degree from Tufts College Medical School in 1939.
His widow and three children survive.

BOSTON MEDICAL LIBRARY

BENJAMIN RUSH AS A SPIRIT

In 1890 Mrs. Cora L. V. Richmond, a medium, published a book entitled *Psychopathy: or spirit healing. A series of lessons on the relations of the spirit to its own organism, and the inter-relation of human beings with reference to health, disease and healing.* The text of this 199-page book was purportedly communicated to Mrs. Richmond by the spirit of Benjamin Rush. The material is divided into nine lessons. Especially interesting are the chapters on psychology, mesmerism, magnetism and electricity as healing agencies; the actual magnetic poles and their corresponding nerve centers; and their relation to psychopathic treatment. Mrs. Richmond also published a book on the soul and at least four volumes of her weekly discourses, containing spiritual sermons communicated by her guides. The business was kept in the family, her publisher being a William Richmond, at least a relative.

MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

NEW DIVISION ANNOUNCED

The section of Health Information of the Department, formerly a part of the Division of Administration, has become a full-fledged division, with Dr. Louis Cohen as director.

One of the new division's first announcements is that the position of director of training, until now financed by a five-year grant from the W. K. Kellogg Foundation, has been made a part of the permanent administrative organization of the Department. Leon A. Bradley, Ph.D., who has been director of training since the division was established in 1950, will continue in the post.

Over 300 public-health workers, according to the report of the division, have already received training in the specialties of medical health administration, medical social work, public-health nursing, health education and environmental sanitation.

A growing need for trained public-health personnel is already evident, with the prospect of an increasing number of Massachusetts communities joining in the formation of local health unions.

CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

The March schedule for Consultation Clinics for Crippled Children in Massachusetts follows:

ORTHOPEDIC CLINICS	DATE	CLINIC CONSULTANT
Salem	March 3	Paul W. Hugenberger
Haverhill	March 5	William T. Green
Greenfield	March 6	Charles L. Sturdevant
Lowell	March 7	Albert H. Brewster
Lynn*	March 10	Daniel M. Killoran John J. Crowley
Gardner	March 11	Carter R. Rowe
Brockton	March 13	George W. Van Gorder
Springfield	March 18	Garry deN. Hough, Jr.
Pittsfield	March 19	Edward J. Coughlin, Jr.
Fall River	March 24	David S. Grice
Hyannis	March 27	Paul L. Norton
Worcester	March 28	John W. O'Meara

RHEUMATIC-FEVER CLINICS	DATES
North Reading	March 4, 11, 18, 25
Fitchburg	March 5, 12, 19, 16

PLASTIC CLINICS	HELD	CONSULTANT
Eastern Massachusetts	Semi-monthly	Bradford Cannon
Western Massachusetts	Monthly	Joseph M. Baker

Physicians referring new patients to clinics should get in touch with the district health officer to make appointments. Patients are seen by appointment only.

*This clinic serves Lynn, Lynnfield, Saugus, Nahant, Revere, Chelsea, Everett and Winthrop. Referrals should be made directly to the Lynn Hospital.

STATE COLLEGE OF KANSAS MAR 7 1952 MANHATTAN

NONCLINICAL NOTES

BUFFALO SURGICAL SOCIETY

On February 14 the Buffalo Surgical Society presented the Roswell Park Memorial Medal for "outstanding surgical achievement" to Dr. Edward D. Churchill, of Boston, Massachusetts.

Dr. Churchill was the fifth recipient of this award. Previous recipients have been Dr. Allen O. Whipple (1948), Dr. Evarts A. Graham (1949), Dr. Dallas B. Phemister (1950) and Dr. Frederick A. Coller (1951).

At the presentation ceremonies, Dr. Churchill delivered the annual Roswell Park Lecture, entitled "The Architectural Basis of Pulmonary Ventilation."

CORRESPONDENCE

HENRY A. CHRISTIAN MEMORIAL LIBRARY

To the Editor: It did our hearts good to see your editorial on "Old Books: New Libraries" in the *Journal* for November 8, 1951, commending the Toledo Academy of Medicine Library for the job it is trying to do. Perhaps you little knew, when you wrote that article, how well the Boston and Harvard medical libraries served as models for our development.

During my internship and resident training at the Peter Bent Brigham Hospital I learned at these institutions the value and proper use of a medical library. But my greatest stimulus came when, in 1938, Dr. Henry A. Christian gave me his personal medical library. I have kept all its journals up to date; I use it constantly and prize it highly.

Now that we are to have a new Academy Library, it is planned, in line with another of your editorials (November 29, 1951), to preserve Dr. Christian's collection in a special part of the building to be called "The Henry A. Christian Memorial Library." I wrote to Dr. Christian of this before he died, and he gave his consent to such a disposition of his collection. As this concerns the proper "Disposition of Rare Book Collections," I thought it might interest you.

MAURICE A. SCHNITKER, M.D., *Director*
Toledo Academy of Medicine Library

Toledo, Ohio

NOTICES

MASSACHUSETTS HEART ASSOCIATION

The Research Allocations Committee of the Massachusetts Heart Association meets bimonthly during the year to review applications for grants-in-aid to institutions for the support of investigations in the field of cardiovascular disease.

In order to be placed on the agenda of any given meeting, applications should be in the hands of the committee at least one week in advance of such meeting. Applications received after the deadline will be placed on the agenda of the following meeting.

All applications may be addressed to Robert W. Wilkins, M.D., Chairman, Research Allocations Committee, Massachusetts Heart Association, 650 Beacon Street, Boston. Each application should be accompanied by a note of endorsement from the administrator of the institution in which the research is to be done.

UNITED STATES PUBLIC HEALTH SERVICE

A competitive examination for appointment of medical officers to the Regular Corps of the United States Public Health Service will be held on June 3, 4 and 5. Examinations will be held at a number of points throughout the United States, located as centrally as possible in relation to the homes of candidates. Applications must be received no later than April 30, 1952.

Appointments will be made in the grades of Assistant Surgeon (equivalent to Navy rank of Lieutenant [j.g.]) and Senior Assistant Surgeon (equivalent to Lieutenant). In making assignments, consideration is given to the officer's preference, ability and experience; however, all commissioned officers are subject to change of station and assignment as necessitated by the needs of the Service. Appointments are permanent and provide opportunities to qualified physicians for a career in clinical medicine, research and public health. Applicants who successfully complete this examination may ordinarily expect appointment as soon as they become eligible.

Application forms and additional information may be obtained by writing to the Surgeon General, United States Public Health Service, Federal Security Agency, Washington 25, D. C. — attention: Division of Commissioned Officers.

NEW ENGLAND SOCIETY OF ANESTHESIOLOGISTS

The New England Society of Anesthesiologists will present a program on "The Physiology of the Central Nervous System and Its Relation to Anesthesia" on March 1, as part of its Postgraduate Education Program.

PROGRAM

The Cerebral Cortex — Dr. Joseph W. D. Garrett, chief of Anesthetic Section, West Roxbury Veterans Administration Hospital.

Somatic Nerves — Dr. Francis X. Mack, visiting anesthesiologist, Boston City Hospital.

The Autonomic Nervous System — Dr. Julia G. Arrowood, chief of service in anesthesiology, Massachusetts Memorial Hospitals.

THE NEW ENGLAND CARDIOVASCULAR SOCIETY

The next meeting of the New England Cardiovascular Society will be presented by the New England Center Hospital and the Children's Medical Center (House of the Good Samaritan and Children's Hospital) on Monday, March 3, at 8:00 p.m., in the Dorothy Quincy Suite of John Hancock Hall, 180 Berkeley Street, Boston.

PROGRAM

NEW ENGLAND CENTER HOSPITAL — Dr. Samuel Proger presiding

Behavior of Serum Lipoproteins During Paper Electrophoresis — Dr. Isadore N. Rosenberg

Experiments With the Grafting of Small Arteries and Veins — Dr. C. Stuart Welch

A Problem in Electrocardiographic Interpretation: Influence of Electrolyte Balance — Drs. William B. Schwartz and Arnold S. Relman

CHILDREN'S MEDICAL CENTER (House of the Good Samaritan and Children's Hospital) — Dr. Benedict F. Massell presiding

Use of Digitalis in Infants and Children: A Clinical Study — Drs. Alexander S. Nadas, Abraham N. Rudolph and John L. D. Reinhold

Cardiac Glycogen-Storage Disease: A Study of Three Siblings — Drs. Benjamin H. Landing, Claude Villee and Alexander S. Nadas

Factors Influencing Recurrences of Rheumatic Fever — Drs. Benedict F. Massell, George P. Sturgis and Joseph M. Miller

BOSTON LYING-IN HOSPITAL POSTGRADUATE COURSE IN OBSTETRICS AND PEDIATRICS

On April 17, 18 and 19 the Boston Lying-in Hospital, in conjunction with the Children's Hospital, will present a new course in obstetrics and pediatrics. This program is designed to acquaint New England physicians with recent advances in knowledge concerning prenatal care and that of newborn infants and those in the subsequent six months of life. The influence of nutrition on mother and infant, diabetes and other medical complications, threatened abortion, abruptio placentae, congenital abnormalities, feeding and immunization will be stressed. These and other subjects will be presented in a two-and-one-half-day program of lectures, conferences, clinical demonstrations, ward rounds and clinicopathological conferences.

Accommodations will permit attendance by 75 physicians. A complete program will shortly be published. Further information may be obtained from Dr. Crawford H. Hinman, 221 Longwood Avenue, Boston 15.

INTERNATIONAL DIABETES FEDERATION

Those interested in the First International Congress of the International Diabetes Federation to be held at Leyden, Netherlands, during the second week of July, 1952, may apply for information to Dr. Elliott P. Joslin, 81 Bay State Road, Boston 15. Completed application forms should be in the possession of the Executive Secretary at The Hague on or before April 1, 1952.

THE SPRINGFIELD HOSPITAL

The Educational Program of the Springfield Hospital for the month of March is as follows:

Saturday, March 1.

10–11 a.m. Surgical Grand Rounds.
11 a.m.–12 m. Combined Medical-Surgical Grand Rounds with Panel Discussion on "The Management of Jaundice," with Dr. William Kaufmann as moderator and the following as discussers: Medical, Dr. Louis Izenstein and Dr. Warren D. Platt; Surgical, Dr. Lewis W. Whiting. Staff Conference Room.

Wednesday, March 5.

11 a.m.–12 m. Group Therapy Conference in the Staff Room.

Saturday, March 8.

10–11 a.m. Surgical Grand Rounds.
11 a.m.–12 m. Clinicopathological Conference in the Staff Conference Room.

Wednesday, March 12.

11 a.m.–12 m. Group Therapy Conference in the Staff Room.

Thursday, March 13.

12:15 p.m. Staff Meeting in the Staff Room.

Saturday, March 15.

9–10 a.m. Colored and sound movie on "Coarctation of the Aorta" by Dr. John C. Jones, associate professor of surgery, University of Southern California Medical School, and on "Tolserol" by Dr. Richard T. Smith, Benjamin Franklin Clinic, Pennsylvania Hospital.
10–11 a.m. Surgical Grand Rounds.
11 a.m.–12 m. Medical Death Review in the Staff Conference Room.

Tuesday, March 18.

8:30 p.m. Guest Speaker Conference in the Staff Conference Room on the subject "Demonstration of the Gull-Strand Slit-Lamp" (Department of Ophthalmology).

Wednesday, March 19.

11 a.m.–12 m. Group Therapy Conference in the Staff Room.

Saturday, March 22.

10–11 a.m. Surgical Grand Rounds.
11 a.m.–12 m. Surgical Death Review in the Staff Conference Room.

Wednesday, March 26.

11 a.m.–12 m. Group Therapy Conference in the Staff Room.

Saturday, March 29.

10–11 a.m. Surgical Grand Rounds.
11 a.m.–12 m. Radiology Conference in the Staff Conference Room on the subject "Pediatric X-Ray Diagnosis." Dr. Robert A. Grugan.

PHI DELTA EPSILON FRATERNITY: SIGMA CHAPTER

The annual lecture of Sigma (Temple) Chapter of Phi Delta Epsilon Fraternity will be given on Monday, March 24, at 4 p.m. in the auditorium of the Temple University School of Medicine. Dr. Franklin F. Snyder, associate professor of obstetrics at Harvard Medical School, will speak on "Breathing Before Birth and Its Obstetrical Significance." All interested persons are invited to attend.

MINNESOTA STATE MEDICAL ASSOCIATION

The ninety-ninth annual meeting of the Minnesota State Medical Association will be held in Minneapolis, Minnesota, May 26–28. All scientific and technical exhibits will be housed in the Minneapolis Municipal Auditorium.

CONGRESS ON MEDICAL LIBRARIANSHIP

An International Congress on Medical Librarianship will be held in London in July, 1953. The program will include formal sessions for reading and discussion of papers, visits to medical libraries and social functions. It is hoped also to have in connection with the Congress an exhibition of medical books and periodicals and library equipment. All those actively engaged or interested in medical librarianship throughout the world are invited to participate. Requests for further information may be addressed in advance to the Honorary Secretary, First International Congress on Medical Librarianship, c/o The London School of Hygiene and Tropical Medicine, Keppel Street, London W.C.1.

SOCIETY MEETINGS AND CONFERENCES

FEBRUARY 23–27 AND MARCH 1–29. Springfield Hospital. Page 204, issue of January 31, and notice above.

FEBRUARY 26. Boston City Hospital House Officers' Association. Page 160, issue of January 24.

FEBRUARY 27–MARCH 26. Lahey Clinic Fellowship Teaching Program. Page 160, issue of January 24.

FEBRUARY 25 AND APRIL 15. Massachusetts Society for Research in Psychiatry. Page 792, issue of November 15.

FEBRUARY 26. Children's Medical Center. Page 280, issue of February 14.

FEBRUARY 26, MARCH 25 AND APRIL 24. Norfolk District Medical Society. Page 710, issue of November 1.

FEBRUARY 28 AND 29. American Psychiatric Association. Page 280, issue of February 14.

MARCH 1, APRIL 5 AND MAY 3. New England Society of Anesthesiologists. Postgraduate Education Course. Page 966, issue of December 20, and page 315 of this issue.

MARCH 2–4. College of Medical Evangelists. Page 280, issue of February 14.

MARCH 3. New England Cardiovascular Society. Page 315.

MARCH 3–5. National Cancer Conference. Page 242, issue of February 7.

MARCH 3–APRIL 30. Seventh Postgraduate Lecture Course. Page 274, issue of February 14.

MARCH 10–13. New Orleans Graduate Medical Assembly. Page 956, issue of December 13.

MARCH 12. Northeastern New York Radiological Society. University Club, Albany, New York.

MARCH 13. Sinusitis. Dr. Francis L. Weille. Pentucket Association of Physicians, 8:30 p.m. Haverhill.

MARCH 24. Annual Lecture of Sigma (Temple) Chapter of Phi Delta Epsilon Fraternity. Notice above.

MARCH 24–28. American College of Chest Physicians. Page 160, issue of January 24.

MARCH 31–APRIL 4. Fifth American Congress on Obstetrics and Gynecology. Page 832, issue of November 22.

APRIL 17–19. Boston Lying-in Hospital. Postgraduate Course in Obstetrics and Pediatrics. Page 315.

APRIL 21–25. Cancer Seminar. Page 114, issue of January 17.

APRIL 23. Massachusetts Academy of General Practice. Springfield.

APRIL 23. New England Obstetrical and Gynecological Society (Spring Meeting). Hartford, Connecticut.

MAY 1–3. American Goiter Association. St. Louis, Missouri.

MAY 20–22. Massachusetts Medical Society. Hotel Statler, Boston.

MAY 26–28. Minnesota State Medical Association. Annual Meeting. Notice above.

MAY 26–29. National Tuberculosis Association. Copley Plaza and Statler hotels, Boston.

JUNE 5–8. American College of Chest Physicians. Page 280, issue of February 14.

JUNE 18–20. Massachusetts Public Health Conference. Amherst.

JULY. Commonwealth and Empire Health and Tuberculosis Conference. Page 792, issue of November 15.

JULY 7–12. International Diabetes Federation. Notice above.

JULY 8–11. Thirteenth British Congress of Obstetrics and Gynaecology. Page 916, issue of December 6.

JULY 14–19. International Congress of Physical Medicine. Page 998, issue of June 28.

SEPTEMBER 7–9. Combined session of the New Hampshire and Vermont State Medical Societies, Mount Washington Hotel, Bretton Woods, New Hampshire.

OCTOBER 29. New England Obstetrical and Gynecological Society. Annual Meeting. Hotel Somerset, Boston.

JULY, 1953. International Congress on Medical Librarianship. Notice above.

(Notices concluded on page xi)